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(54) Title: CYCLODEXTRIN CONTAINING PRESSURE SENSITIVE ADHESIVES

(57) Abstract: Compositions are disclosed which are normally pressure sensitive adhesive at ambient temperature, which are also absorbent of fluids, especially body fluids, and which contain 0.1 to 65 wt.% of a cyclodextrin material. Such compositions have various uses in the medical field. Lower amounts of cyclodextrin, from 0.1 - 10 wt.%, can confer odour absorbing properties on the adhesive, useful in consumer and medical products. Small amounts of other active ingredients such as antimicrobial components, active drug ingredients, fragrances, etc. may advantageously be complexed within the cyclodextrin molecules. Such compositions are useful for example as antibacterial adhesives, or as adhesives that bleach the skin, prevent and diminish acne skin blemishes, or provide a cooling or warming sensation to the skin. Higher amounts of cyclodextrins, up to 65 wt.% of the composition, either alone or in combination with other absorbent fillers to total up to 65 wt.%, find utility especially as barrier adhesives for ostomy patients and as wound dressings, and are particularly useful in that they provide fluid absorbent adhesives that also possess odour absorbing properties. Such adhesives are particularly useful as ostomy adhesives.

CYCLODEXTRIN CONTAINING PRESSURE SENSITIVE ADHESIVES

This invention relates to pressure sensitive adhesive compositions containing cyclodextrins. By the term "pressure sensitive adhesive" is meant those adhesives that have touch perceivable tack, that are easily deformed in the time scale allowed for bond formation and that are capable of being applied and bonded to the substrate at temperatures no higher than about 50°C, and preferably at ambient temperatures. Pressure sensitive adhesives are employed in many fields. Pressure sensitive adhesives are used, *inter alia*, as components of labels, industrial tapes, postage stamps, stationery products, and in medical products such as surgical drapes, tapes, ostomy products, wound care products and devices for transdermal drug delivery.

This invention relates particularly to pressure sensitive adhesives used in contact with skin and more particularly to the class of medical pressure sensitive adhesives that are generally termed hydrocolloid adhesives. Most particularly, the invention relates to adhesives that are able to absorb odours associated with body fluids and/or wounds, and to adhesives that have improved ability to deliver active ingredients to wounds or skin.

Hydrocolloid adhesives are a unique kind of medically useful pressure sensitive adhesive. They have usually two phases - a rubbery phase which provides pressure sensitive tack, sometimes called "dry tack" and, dispersed within the continuous rubbery phase, a discontinuous phase of absorbent material. Depending upon the nature of the absorbents, and especially whether the absorbent is soluble in aqueous media or merely swellable, the adhesive composition can develop "wet

tack" as it becomes imbibed with fluid. Such wet tack can also influence the adhesive power of the hydrocolloid. Hydrocolloid adhesives thus have a duality of attributes in that they are inherently adhesive and inherently absorbent. They are useful as wound dressings because they can be applied directly to open wounds and can be secured on the surrounding intact skin, and as skin barriers because they protect the peristomal skin of ostomy patients. Hydrocolloid adhesives maintain the skin in a normally or optimally hydrated condition. Optimally hydrated skin is less subject to irritation and injury from repeated application and removal of adhesives than is macerated skin, which latter can result from the use of conventional pressure sensitive adhesives on the skin.

Many hydrocolloid skin barriers are known and are used especially in the fields of ostomy care and wound care. It is convenient to divide these into "integrated" compositions and "non-integrated" compositions. In this context, "integrated" means those compositions that substantially retain their dimensional stability and form when saturated with wound exudate and/or other body fluid. Integrated hydrocolloids usually contain cross-linked or pseudo cross-linked rubbery matrices in the continuous phase to provide the integrating network. But specific combinations of absorbents have also been reported to give highly integrated hydrocolloids, even in the absence of a cross-linked rubbery matrix. "Non-integrated" means those compositions which become soft gels and amorphous as they become saturated with fluid. In this invention, both integrated and non-integrated hydrocolloids are encompassed.

It is often desired to add small quantities of an agent to a medical pressure sensitive adhesive to confer additional benefits. For example, skin problems are common for persons

who have a stoma, which is an artificial body opening produced as a result of surgery. PCT Application WO 98/01167 discloses in this regard a hydrocolloid pressure sensitive adhesive containing an amount of aloe vera up to 5wt% which is said to offer a better protection of the skin against the aggressive action of excreted substances. Again, in European Patent Specification No. 0 023 395 B1, mention is made of pressure sensitive adhesives containing a broad spectrum antimicrobial agent. In this prior art, the antimicrobial agent is dissolved in a suitable solvent and dispersed in the said pressure sensitive adhesive to give a two-phase system, which is said to release the antimicrobial agent in a controlled way.

If the context permits, we use in this Application the term "hydrocolloid" to embrace the term "cyclodextrin", and within the scope of the invention a cyclodextrin may be or may not be the only hydrocolloid present in the adhesive.

According to a first aspect of the present invention there is provided a pressure sensitive adhesive composition comprising a rubbery continuous phase and a discontinuous phase, wherein the discontinuous phase comprises 0.1 to 65 wt%, preferably at least 5 wt% of a cyclodextrin material, and optionally a hydrocolloid other than a cyclodextrin, said percentages being based on the total composition. The preferred minimum of cyclodextrin in a composition according to this aspect of the invention is 10 wt%. The discontinuous phase in total preferably comprises 5 to 70wt% of the total composition, more preferably 10 to 60wt%.

A further aspect of the present invention relates to constructions comprising a layer of cyclodextrin containing hydrocolloid adhesive that further contains an effective

amount of one or more active ingredients. Hydrocolloid adhesives are particularly suitable as the basis for such constructions, because of their ability to maintain the skin in a normally or optimally hydrated condition. Often, such skin patches will be applied to the skin over an extended period, and hydrocolloid adhesives will maintain the skin in a healthy condition. As non-limiting examples of what is contemplated, the active ingredient may be an antibacterial or antifungal compound, a compound such as hydroquinone, a compound such as an essential oil, for example tea tree oil, or mixtures of essential oils, a compound such as salicylic acid, a compound such as menthol, or a fragrance composition. Hydrocolloid adhesives containing such active ingredients can be made into, for example, skin patches that will deliver the active ingredient to the skin surface. The advantage of using cyclodextrin complexes of these active ingredients is that often the active ingredients are labile, or not soluble, or not stable, or may interact with other ingredients in the formulation. Inclusion of these active ingredients within the molecular structure of the cyclodextrins provides an effective way of insuring delivery to the target skin site. It will be understood that, within the scope of the invention, the active ingredient does not have to be complexed within the cyclodextrin molecule - it can also be present in a free, or uncomplexed, state. The cyclodextrin will function in such cases as odour absorbing means, and/or as absorbing means. In the case of compositions containing more than one active ingredient, again the complexing of one or more of the active ingredients within a cyclodextrin molecule is optional.

Complexing is a preferred feature however, and according to a further aspect of the invention there is provided a pressure sensitive adhesive composition containing 1 to 10 wt%

of cyclodextrin, all or part of which is complexed with one or more active ingredients of this composition.

Non-limiting examples of prior art hydrocolloid compositions suitable for use as bases for the reduction to practise of the present invention, with appropriate modification in accord with the teachings herein described, are given in US Patent 3,339,546, US Patent 4,231,369, US Patent 4,477,325, US Patent 4,738,257, US Patent 4,551,490, US Patent 4,192,785, US Patent 4,952,618, all of which patents are incorporated herein by reference.

The present invention also provides skin barriers and wound dressings comprising a layer of hydrocolloid adhesive containing an effective amount of a cyclodextrin and which is backed by a non-adhesive, waterproof film to form a skin barrier or dressing. The skin barrier is used in a number of ways. One of these is for wound dressing purposes. Patients in institutional settings such as hospitals and nursing homes often have or acquire chronic wounds such as venostasis ulcers and bed sores, and these wounds can possess a very offensive odour. Bandages or dressings made from or incorporating the compositions of the invention are able to absorb odour molecules and thereby reduce or eliminate the offensive odour. This contributes to the well-being of the patient as well as to the nursing staff and other patients, since the odours from chronic wounds can be offensive to both carers and to family members of the patient. Another important use is for the protection of the skin around body openings, especially around the surgically created openings known as colostomies, ileostomies and urostomies. Collectively, these surgically created body openings are often termed stomas. The novel skin barriers of the invention are able to absorb the odour

molecules that are associated with faeces and urine and thus are able to assist in the control of the odour that is associated with stomas. This can increase the self-confidence of the patient because such odours can be a source of personal embarrassment. While not wishing to be bound by any particular theory, it is believed that the cyclodextrin molecules are able to absorb malodorous molecules, which become complexed within the toroidal structure of the cyclodextrin molecule.

One yet further aspect of the invention relates to incorporation of cyclodextrin materials into pressure sensitive adhesives based on hydrophilic polymers, which will usually, though not necessarily, be crosslinked. These materials are commonly termed hydrogels, and can form the basis of medical pressure sensitive adhesives. With hydrogels, the pressure sensitive adhesive property is achieved by plasticisation of the polymer with water and/or a hydrophilic plasticiser, and thus the cyclodextrin may or may not be completely dissolved in the pressure sensitive adhesive, depending on whether the cyclodextrin is completely soluble in the plasticising medium. Thus, the possibility exists with this adhesive system for a cyclodextrin containing pressure sensitive adhesive that has only one phase.

Adhesives containing fragrance compositions are very useful to mask the bad odours associated with the presence of urine and faeces on the skin, which can occur with ostomy patients. Often, fragrances can be irritating to the skin, or can cause allergic reactions. When the fragrances are first complexed with a cyclodextrin material, the fragrance is released when the cyclodextrin becomes moist, and the amount liberated is controlled by the rate and amount of moisture ingress. In this way, any irritation potential or allergic

response with the particular fragrance is minimised or eliminated.

The introduction of cyclodextrins, in combination with certain "active compounds", into pressure sensitive adhesives is known and is reported in the prior art.

For example Japanese Patent Application JP 6158002A, to Sekisui Plastics Co., describes an antibacterial pressure sensitive adhesive for food containers, wherein isothiocyanuric acid ester is complexed within β-cyclodextrin and added to a pressure sensitive adhesive which is then adhered to the inside surface of the food container to control bacterial and fungal growth.

US Patent 5,352,717 to American Maize Technology Inc. teaches adhesive or sealant compositions containing a small amount of cyclodextrin. Some examples also have, as an optional component, a blowing agent to expand the adhesive to a foamed material for industrial uses. Although one of the examples talks to a "pressure sensitive adhesive", the exemplified adhesive is said to be applied at temperatures of 160°C., as are the other examples, which are clearly directed at hot melt adhesive compositions, outside the contemplated area of interest of the instant invention.

US Patent 4,978,532 to Pharmedic Co. describes a dosage form for the administration of dehydroepiandrosterone (DHEA). The dosage form comprises a medical grade silicone pressure sensitive adhesive, DHEA and a permeation enhancer, an example of which is hydroxypropyl-β-cyclodextrin.

Also of interest is the US Patent 5,562,917 to Pentech Pharm Inc. that claims a composition suitable for the treatment of Parkinson's disease involving the transdermal delivery of apomorphine in an aqueous based gel. Specified is a permeation enhancer which includes hydroxypropyl-β-cyclodextrin. Also specified is a matrix of silicone copolymer pressure sensitive adhesive, 0.1 - 3wt% of apomorphine and a carbocyclic compound having pendant hydroxyl groups selected from butylated hydroxy anisole, butylated hydroxy toluene and hydroxypropyl-β-cyclodextrin as a permeation enhancer.

The use of cyclodextrins in cosmetics as odour absorbing agents and as vehicles to deliver active ingredients to, for example, the skin, is known in the literature. For example, PCT Applications WO 98/56343 WO 98/56344 and WO 98/56345 disclose cosmetic compositions for topical application to the skin that contain an aqueous phase or a water-in-silicone emulsion, a cyclodextrin compound and a salicylic acid derivative. Such compositions are said to provide anti-acne and anti-inflammatory activity together with reduced skin irritation.

PCT Application WO 99/06078 discloses cyclodextrin odour absorbent articles for decreasing odours associated with body fluids, where the cyclodextrin has a specific particle size. PCT Application WO 98/56890 teaches the combination of aqueous cyclodextrin compositions with wrinkle control agents for odour and wrinkle control of fabrics. PCT Applications WO 98/17239, WO 98/17240, WO 98/56341 and WO 98/56342 describe an aqueous carrier containing soluble cyclodextrins, perfume compositions and preferably hydrophobic antimicrobial compounds in order to reduce body odour and or environmental odour. PCT Applications WO 98/18439 and WO98/56340 reveal

similar compositions in a powder carrier such as a starch. PCT Application WO 98/56339 describes similar compositions in a two phase formulation comprised of an aqueous phase and an oil phase.

US Patent 5,429,628 and PCT Application WO 94/22501 both teach the preparation of articles containing small particle size cyclodextrin for odour control. A large number of consumer absorbent products, such as panty liners, catamenials, diapers and sanitary napkins are exemplified, where the cyclodextrin is present within, or as part of, a fibrous absorbent medium.

European Patent Specification 0 392 608 B1 concerns solid consumer product compositions containing an ingredient such as a flavour, a drug or a perfume that is complexed within a cyclodextrin. Product categories that are mentioned include those such as drinks and beverages, canned pet foods, cosmetics and toiletries such as facial scrubs, body powders, depilatories, mouth washes and lipsticks, detergents, paper towels, cake mixes and cookies, incense, room deodorant blocks, dyes, insect repellents and the like.

PCT Patent Application WO 94/18973 discloses the complexing of bisacodyl with cyclodextrin to provide an oral dosage form that delays the laxative action of the bisacodyl until the preparation is near the junction of the small intestine and the colon.

US Patent 5,246,611 and PCT Applications WO 93/05136 and WO 91/17300 all deal with the use of cyclodextrin perfume complexes in fabric treatment products such as fabric softeners. The cyclodextrin complexes are suspended in

polyalkylene glycol carrier which does not prematurely displace the active from the cyclodextrin.

What becomes evident from a reading of the prior art is that, notwithstanding the very great amount of art that exists concerning cyclodextrin containing materials, nowhere in the literature is reported the use of cyclodextrins as an integral component in pressure sensitive adhesive compositions.

Concerning odour absorbent adhesives, there appears to be little or no prior art. Japanese Application 10168348A to Kodaijin Sugaoka KK does disclose incorporation of cristobalite as a component of wall coatings which also contain pressure sensitive adhesives, and the cristobalite is said to absorb foul odours. But the finished composition is not itself pressure sensitive adhesive; indeed, it is said to resemble Japanese lime plaster.

McNeil-PPC Inc. in US Application 93168550 A disclose panty liners in which a pressure sensitive adhesive is applied to an absorbent structure containing baking soda to absorb odours. Plasto SA, in German Application 19724871 A1, claim a laminated structure comprised of a polyolefin film having dispersed in it a perfume, and coated on one side with a pressure sensitive adhesive. Such a structure will obviously serve only to mask an odour, and the perfume is in the film, not in the adhesive. Schering Plough in US Patent 5,399,404 teach a patch for masking foot odours comprising a carrier on one side of a non-occlusive layer which contains fragrance and a pressure sensitive adhesive on the other side of the carrier to secure the patch to the foot or shoe. In PCT WO 9423766 A1, Schering Plough also disclose a deodoriser for masking foot and shoe odours comprised of a pressure sensitive adhesive

laminated to a felt which contains a perfume. Kock in Canadian Application 2041278 A describes a disposable perspiration absorbing pad which can be adhered to clothing and adjusted in size and shape and which contains an odour absorbing or perfumed layer.

In none of the above prior art is there any reference or suggestion that the pressure sensitive adhesive component is itself odour absorbing, or which itself delivers a perfume.

What is surprising and unexpected in the instant invention is that, if cyclodextrins are employed as the integral absorbant filler, or as part of the integral absorbent fillers, in hydrocolloid adhesives, the resulting compositions have a unique and wide versatility. They are capable of adhering to surfaces, absorbing fluids, absorbing odours, providing a fragrance and delivering active substances. There is no indication or suggestion in the literature to add or incorporate cyclodextrins into hydrocolloid adhesives, nor any indication or suggestion that such addition should yield the advantageous results of odour control and reduction. Further, is there no suggestion or indication that fragrances and many active ingredients may advantageously be delivered to the skin by incorporating them into such cyclodextrin containing hydrocolloid adhesives.

The adhesive of the invention comprises any suitable pressure sensitive adhesive matrix known in the art and having hydrocolloid particles and/or cyclodextrins dispersed or dissolved therein. The permanently tacky pressure sensitive adhesive component must be tacky at room temperature as well as at the skin temperature of patients. Also, the adhesive must be dermatologically acceptable, which means that after

continuous contact with skin there is little adhesive residue upon removal and there is no significant reaction with the skin during the adhesion period. The adhesive strength of the continuous phase must be sufficient to adhere to the skin of the patient for the time determined by the use of the medical device of which the adhesive forms part. Other ingredients such as tackifiers, plasticisers, and polymer stabilisers may be added to the continuous rubbery phase, to modify tack and optimise adhesion properties and to protect polymers from degradation during processing.

The adhesive matrix may be based on for example polyisobutylene, butyl rubber, polyacrylates, polyurethanes, silicone gum, natural gum rubber, SBR rubber or polyvinyl ether. Thermoplastic elastomers such as styrene-isoprene-styrene block copolymers and styrene-ethylene/propylene-styrene block copolymers may be used, and these may require optional tackifiers and plasticisers. Blends or mixtures of elastomers may be employed. Conventional additives such as tackifiers, softeners, plasticisers and antioxidants may be present to modify, adjust and stabilise the adhesive and other properties of the matrix. The amount of adhesive matrix with respect to the total composition will generally be from 35wt% to about 99wt% or more. Hydrophilic polymers, such as are used in hydrogels, may also form the basis of the pressure sensitive adhesive matrix.

Suitable hydrocolloids for use in the adhesives in conjunction with the cyclodextrins are naturally occurring hydrocolloids such as pectins, guar gum, karaya gum, locust bean gum, carageenan, tragacanth gum, alginates, xanthan gum, modified naturally derived substances such as sodium carboxymethyl cellulose, synthetic materials such as

polvinylalcohol, polyoxyalkylene polyols, polyvinyl pyrollidone, and animal derived materials such as gelatine. Ionic hydrocolloids such as hyaluronic acid, chitosan salts or DEAE Dextran may also be employed. The hydrocolloids may be water absorbable or water swellable, and combinations of one type or of various types may be used in any ratio. A hydrocolloid in addition to cyclodextrin may be used in an amount from 0wt% to 60wt% or more, and when combined with the cyclodextrin component the aggregate of the two will amount to from 0.1wt% to 65wt%.

The term cyclodextrin, as used herein, includes any of the known cyclodextrins. Cyclodextrin materials are cyclic oligosaccharides containing a minimum of six D-(+)-glucopyranose units attached by α- (1 > 4) glucosidic bonds. Three cyclodextrins called α, β and γ are naturally occurring and have, respectively, six, seven and eight glucose units. Cyclodextrins are known that contain up to twelve glucose units. Cyclodextrin materials can also be manufactured from starch by enzymatic degradation. In addition, many synthetic modifications of the natural material materials are known, for example methyl-β-cyclodextrin and hydroxypropyl-β-cyclodextrin. The conformations of the cyclic structures of these molecules are such that the molecules are arranged in rigid conical molecular shapes that have hollow interiors of very well defined sizes. These internal cavities are hydrophobic in nature because the interior of the toroidal shape is predominantly made up of hydrogen atoms. The interior shapes of the cyclodextrins are able to form inclusion complexes, sometimes referred to as "host-guest" complexes, or clathrate compounds, with organic molecules which fit, completely or partially, into the cavities defined by the toroidal shapes. For example, odiferous molecules can fit into

the cavities. This includes both perfumes and malodorous compounds. Cyclodextrins therefore, and especially mixtures of cyclodextrins with cavities of different sizes, can be used to control odours. With respect to odour control, there is scope for two different approaches within the present invention. First, uncomplexed or free cyclodextrins, dispersed within the adhesive matrix, can be used to absorb malodours. Second, perfumes can be precomplexed with cyclodextrins and then formulated in the final adhesive. The perfume is then released *in situ* and will mask the undesirable odour. (Once a cyclodextrin molecule has released its precomplexed perfume molecule, it is then available to complex a malodorous molecule). The complexation of odorous molecules by cyclodextrin and the release of precomplexed perfume molecules from cyclodextrin are facilitated by the presence of water. It will be understood that the water necessary to facilitate such release of perfume and complexing of malodour by the cyclodextrin is present in the contaminating urine or faeces, and/or is released by the skin through normal transpiration, and will be absorbed by the adhesive.

The choice of cyclodextrin employed in a given formulation will be decided on the basis of the properties desired in the finished product, and the specific role that the cyclodextrin is fulfilling. Unmodified β-cyclodextrin is not very water soluble and is generally not preferred if high absorbancy is needed. α-cyclodextrins, γ-cyclodextrins and certain modified β-cyclodextrins are more water absorbent. Mixtures of cyclodextrins are often preferred, because these will absorb a wider range of malodorous molecules than will a single cyclodextrin. The cyclodextrin to be used for a specific complex will of course be determined by the size and shape of the active molecule to be complexed.

Any active ingredient may be considered for addition to the formulations anticipated by the instant invention. By active ingredient, we mean an ingredient that is not essential to the functioning of the formulation as a moisture and odour absorbing pressure sensitive adhesive. An active ingredient is added to confer an additional benefit to the formulation. It is not necessary that the active ingredient first is complexed with a cyclodextrin prior to mixing into the formulation, nor indeed that it complexes with a cyclodextrin at all, although it will generally be advantageous if the active ingredient is so complexed. The following active ingredients exemplify the scope of the invention, and represent a non-limiting list of active ingredients.

Aspirin, benzocaine, benzyl alcohol, butamben picrate, camphor, camphorated metacresol, chloral hydrate, chlorabutanol, chloraxylenol, cyclomethycaine sulphate, dibucaine, dibucaine hydrochloride, dimethisoquin hydrochloride, diphenhydramine hydrochloride, dyclonine hydrochloride, eugenol, glycol salicylate, hexyl resorcinol, hydrocortisone, hydrocortisone acetate, juniper tar, lidocaine, lidocaine hydrochloride, menthol, methapyrilene hydrochloride, phenol, phenolate sodium, pramoxine hydrochloride, resorcinol, resorcinol monoacetate, salicylamide, tetracaine, tetracaine hydrochloride, thymol, triethanolamine salicylate, tripelennamine hydrochloride, allyl isothiocyanate, ammonia, capsaicin, eucalyptus oil, histamine dihydrochloride, methyl nicotinate, methyl salicylate, turpentine oil, allantoin, calamine, dimethicone, glycerin, kaoline, petrolatum, shark liver oil, zinc acetate, zinc carbonate, zinc oxide, hydroquinone, quinine sulphate, vitamine E, pregnenolone acetate, progesterone, salicylic

acid, clioquinol, haloprogin, miconazole nitrate, tolnaftate, undecylenic acid, benzoyl peroxide, sulphur, povidone iodine, benzalkonium chloride, benzethonium chloride, methylbenzethonium chloride, trichlosan, trichlocarban, chlorhexidine gluconate, bacitracin zinc, neomycin sulphate, glycolic acid, tea tree oil, lavender oil.

Active ingredients must be present at sufficient concentrations to achieve the desired effect. In general, however, active ingredients will be present usually at no greater than 10wt%, and preferably at no greater than 5wt%, with respect to the total composition.

Other components such as chemical agents that facilitate release of active ingredients from the adhesive formulations, for example plasticisers and solvents for the active ingredients be optionally be present. Also agents that promote absorption of active ingredients by the skin, may optionally be added to the formulation. Non-limiting examples of such skin permeation enhancers are isopropyl myristate, oleic acid, propylene glycol and laurocapram. Other optional ingredients such as small amounts of pigments or colourants may also be present in the compositions.

Test Methods

The formulations in the examples below were evaluated using the following test methods.

Reverse tack

Reverse tack of hydrocolloid adhesives is the maximum force necessary to remove a standard polyester strip brought into

contact with the hydrocolloid without external force, from this hydrocolloid surface.

Procedure

Make the test panel self adhesive using double coated tape. Laminate the hydrocolloid adhesive on the test panel. Place the test panel with hydrocolloid in the lower clamp of a tensile testing machine. Program the tensile tester. Place a polyester test strip of thickness 125 μ (5 mils) and dimensions (21 cm x 2.54 cm) in the upper clamp, making sure that the total length of polyester under the clamp (loop) is 15 cm. Remove the release liner from hydrocolloid and start the measurement.

The reverse tack is the maximum force to remove the polyester strip from the hydrocolloid surface.

90° Peel adhesion of hydrocolloid adhesives on SS

Peel adhesion on stainless steel (SS) is the average force to remove a hydrocolloid adhesive, laminated under specified conditions on a SS panel, from the SS panel at constant speed and at an angle of 90°.

Procedure

Clean the SS-panel with solvent. Cut a hydrocolloid sample of 25.4mm width and reinforce with reinforcing tape, laminate a paper strip at one end of the hydrocolloid sample using an overlap of about 1 cm. Remove the liner from the hydrocolloid sample and laminate the sample on the SS-panel with a 450 gm. roller at a speed of 150 cm/min. Allow the sample to dwell for 1 minute. Place the paper strip in the upper clamp and the SS-panel on the lower clamp, making sure that the angle between peel direction and SS-panel is 90°. Start the measurement

using a crosshead speed of 300mm/min. The angle must be kept 90° until the measurement is completed. The 90° peel adhesion is the average force to remove the hydrocolloid strip from the SS-panel.

Static shear of hydrocolloid adhesives

Static shear is the time necessary to remove a hydrocolloid adhesive, laminated on a stainless steel panel under specified conditions, from the test panel under influence of a specified weight.

Procedure

Condition the hydrocolloid samples at 23 ± 1° and 50 ± 2% relative humidity for 24 hours. Clean the SS shear panel with solvent. Cut a hydrocolloid strip of 25.4 mm width and 50 mm length. Reinforce the hydrocolloid strip with reinforcing tape. Laminate the hydrocolloid strip on the test panel using an overlap surface of 1 inch². Protect the free hydrocolloid with release liner. Put a weight of 500 g on the laminate for 1 hour. Reinforce the free hydrocolloid adhesive zone with reinforcing plastic and perforate. Place the test panel with hydrocolloid on the shear bar using a shear weight of 500 g. Re-zero the registration-clock. Note the time on the clock when sample falls off under the influence of the 500g. Weight. This completes the measurement.

Static absorption of hydrocolloids.

To determine the amount of fluid uptake into a known surface of hydrocolloid adhesive.

Procedure

Laminate release liner to the upper flange of a moisture vapour transmission determination cup with the double coated

tape. This is the contact zone for the hydrocolloid. Fill the cup with 30 ml NaCl solution (0.9%wt). Cut a sample of hydrocolloid of about the same size as the outer cup diameter. Weigh the sample (W_1). Laminate the sample to the cup, making sure that the seal between the hydrocolloid sample and the cup is water tight. Turn the cup upside down and put it in the oven at 37°C. for 24 hours. Cool down. Remove the hydrocolloid from the cup and reweigh (W_2). Calculate the water fluid absorption (g/sq.m.24h) using the formula :

$$abs = (W_2 - W_1) / 0.002375$$

where the area of the hydrocolloid in contact with salt solution is 0.002375 sq.m.

Determination of cold flow

The flow of the hydrocolloid under influence of a specified pressure and after a specified time, is measured.

Procedure

Condition the hydrocolloid samples at 23 ± 1°C and 50 ± 2 % relative humidity for 24 hours. Cut 5 samples of hydrocolloid using a 35mm circular die-cutter. Put a silicone paper on top of a first glass plate. Arrange the 5 samples on the silicone paper in a way that pressure is distributed equally. Measure the diameter of each sample with callipers, mark the exact place where the measurement is done. Put a plastic disk on each sample. Put another silicone paper and two glass plates over the construction followed by a weight of 10 kg. (The measurement can also be done by placing the sample with the disk and the 10kg. weight in an oven maintained at 40°C). After 24 hours, measure the diameter of the samples where they are marked. Calculate the % increase of

diameter of the samples. The cold flow is the % increase of diameter after 24 hours exposure to 10 kg (for 5 samples). Record the % increase in diameter and the test temperature.

Determination of the integrity of hydrocolloids

The integrity of a hydrocolloid is defined as its ability to resist breakdown by biological fluids. The test measures the weight percentage of hydrocolloid adhesive retained after exposure to saline under specified conditions.

Procedure

Condition the hydrocolloid samples at 23 ± 1°C and 50 ± 2 % relative humidity for 24 hours. Cut circular samples 2.54cm in diameter from hydrocolloid sheet. Weigh and record the samples (W_i). Place each sample in a bottle with 50ml aqueous saline (0.9%wt). Cap the bottles and agitate on the bottle shaker at 400 speed for a period of 18hrs. Remove the sample and dry it in the circulating air oven at 50°C and 50% relative humidity until dry. This takes about 24 hours. Weigh and record the sample (W_f). The Integrity Value of the sample is calculated using the following equation:

$$\text{Integrity Value (\%)} = 100 \times \frac{(W_f)}{(W_i)}$$

A complex of γ-cyclodextrin and triclosan was formed by allowing a suspension of triclosan in an aqueous solution of γ-cyclodextrin (molar ratio 1.25 γ-cyclodextrin: 1.0 triclosan) to equilibrate for 24 hours at 25°C. with constant stirring. At equilibrium, a dense white precipitate corresponding to a 1:1 stoichiometric ratio of γ-cyclodextrin to triclosan was formed.

A complex of citral in β-cyclodextrin was prepared by mixing 200ml water and 62gm β-cyclodextrin at room temperature. Citral (7.6gm) was added dropwise to the suspension of β-cyclodextrin. After intensive stirring at room temperature for about 10 hours, the suspension was allowed to stand for a further 24 hours. The complex was filtered and vacuum dried at 40°C.

A complex of citral in γ-cyclodextrin was prepared by dissolving 70gm γ-cyclodextrin in 200ml water at 50°C, and adding citral (7.6gm) dropwise to the γ-cyclodextrin solution. After intensive stirring at 60°C for about 6 hours, the solution was allowed to stand for a further 24 hours. The complex was filtered and vacuum dried at 40°C. The concentration of citral in the γ-cyclodextrin complex was 11wt%.

A complex of evening primrose oil in γ-cyclodextrin at a level of 15wt% oil was prepared by dissolving 70gm γ-cyclodextrin in 200ml water at 45°C, and adding the evening primrose oil dropwise to the γ-cyclodextrin solution. Stirring was continued for 6 hours, and the complex was allowed to cool

and stand for a further 24 hours, after which time it was filtered and dried *in vacuo*.

The invention will now be further described with reference to the following non-limiting examples.

Examples 1 - 4

These examples illustrate a cyclodextrin containing hydrocolloid adhesive suitable for a WC flushable ostomy pouch. This flushable requirement means that the hydrocolloid should not be integrated, so that it will disintegrate satisfactorily in the sewage system. Example 1 is a hydrocolloid containing polyisobutylene, pectin, gelatine and sodium carboxymethyl cellulose, which was made as a control material. This hydrocolloid, described in US Patent 3,339,546, is an inelastic, non-integrated hydrocolloid adhesive which has been on the market as an ostomy barrier material and as a wound dressing material for many years, and is considered a standard product.

Each formulation was prepared in a 500gm batch in a 1l. Z-blade mixer. The pectin, the sodium carboxymethyl cellulose and the third powder was added to the mixer at 90°C and the powders blended together for 2 minutes. Then the Vistanex LMMH was added to the powders and the formulations were further mixed for 30 minutes at 90°C. The finished hydrocolloid adhesives were made into sheets of approximately 1mm thickness by pressing about 130gm of each formulation between two sheets of silicone release paper in a hydraulic press at 90°C.

Wt% of Each Raw Material	Ex. 1	Ex. 2	Ex. 3	Ex. 4
Polyisobutylene, Vistanex LMMH	40.6	40.6	40.6	50.0
GenuPectin USP 100	19.8	19.8	19.8	-
Sodium CMC, Blanose 7H4XF	19.8	19.8	19.8	-
Gelatine 100 mesh, 225 Bloom	19.8	-	-	-
β-Cyclodextrin (Cavitron 82000)	-	19.8	-	-
Hydroxypropyl β-Cyclodextrin (Cavitron 82005)	-	-	19.8	50.0
Totals, wt%	100	100	100	100

Physical Data	Ex. 1	Ex. 2	Ex. 3	Ex. 4
Reverse Tack, N/25mm	17.5	21.5	20.3	18.7
Peel Adhesion, 90°/ Stainless Steel, N/25mm	8.8	7.9	12.0	15.0
Shear, 0.5kg, minutes	94	68	58	43
Thickness,mm	1.27	1.20	1.06	1.00
Static Absorption, gm/sq.m./24hr	7280	7242	7301	177
Cold Flow, % increase/24hr/10kg	7.2	18.7	11.7	18.6
Integrity, %, 6hr	65	82	58	97

Example 5

The hydrocolloid adhesive of Example 3 is laminated to a spun laced nonwoven fabric which had previously been waterproofed and coated with a medical grade acrylic pressure sensitive adhesive. The acrylic adhesive functions as a tie layer to bond the hydrocolloid adhesive to the polyester fabric. Such an acrylic adhesive coated nonwoven fabric is available commercially from Smith & Nephew plc as Lasso SA72.

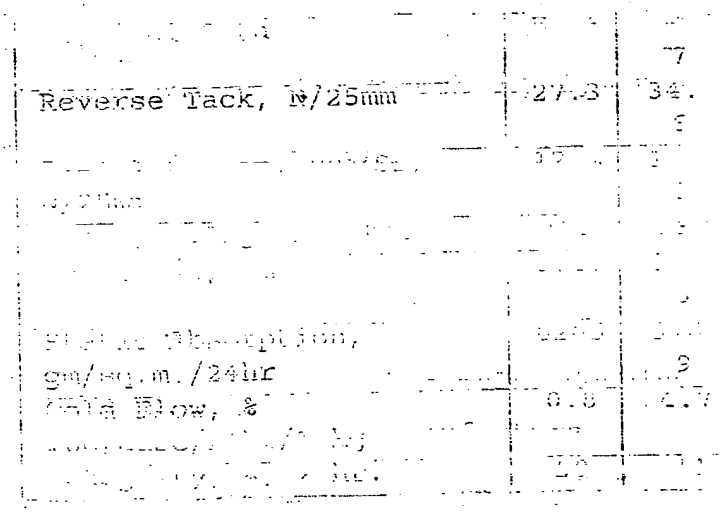
The skin barrier so produced is made up into a drainable ostomy pouch having a stoma hole size of 32mm. The stoma pouch is used by a 22 year old ileostomy patient who is experiencing leakage problems with his commercially available pouch. The hydrocolloid adhesive of Example 3 has a high cold flow value, which means that the adhesive flows easily into the scarred depression on the patient's abdomen close to the stoma.

Although the hydrocolloid on the stoma erodes somewhat within 24 hours, the pouch adheres well, and the adhesive absorbs the odour caused by faecal contamination at the edge of the adhesive exposed close to the stoma opening. The patient is pleased with the performance of the pouch, and states that there is less odour noticeable with the pouch of example 5 compared to his current commercially available pouch.

Examples 6 - 8

Examples 6 - 8 show the effect of substituting cyclodextrins for one ingredient in a moderately integrated hydrocolloid formulation suitable for use as a hydrocolloid wound dressing. Aqualon A-500, which is a crystalline sodium carboxycellulose, was substituted with cyclodextrin material. 500gm batches of each formulation were prepared. The polyisobutylene (Vistanex LMMH), the Pectin, the Blanose sodium CMC and the third powder were added at 90°C to a 1l. Z-blade mixer. After mixing for 15 minutes at 90°C, the temperature was raised to 100°C, and the other ingredient, the preformulated hot melt adhesive, was added and mixed for a further 30 minutes.

The Kraton KD-1161NS is a blend of linear styrene/isoprene/styrene triblock copolymer and linear styrene/isoprene diblock copolymer. Such a material is available from Shell Chemical Company and has a bound styrene content of about 15% and a diblock content of 17%. The mixture of tackifying resins used was a cyclopentadienyl resin, Escorez 2203LC, available from Exxon Chemical, and Adtac LV-E, a C5 synthetic hydrocarbon resin available from Hercules Chemical Company. The Irgafos 168 is an organophosphite stabiliser available from Ciba while the Irganox 565 is a hindered phenolic antioxidant also available from Ciba.



Wt% of Each Raw Material	Ex 6	Ex 7	Ex 8
Polyisobutylene, Vistanex LMMH	28.0	28.0	28.0
GenuPectin USP 100	14.0	14.0	14.0
Sodium CMC, Blanose 7H4XF	14.0	14.0	14.0
Sodium CMC, Aqualon A-500	14.0	-	-
β-Cyclodextrin (Cavitron 82000)	-	14.0	-
Hydroxypropyl β-Cyclodextrin (Cavitron 82005)	-	-	14.0
Kraton D-1161NS	11.3	11.3	11.3
Adtac LV-E	6.0	6.0	6.0
Escorez 2203 LC	12.5	12.5	12.5
Irgafos 168	0.14	0.14	0.14
Irganox 565	0.07	0.07	0.07
Total	100	100	100

Physical Data	Ex 6	Ex 7	Ex 8
Reverse Tack, N/25mm	27.3	34.6	23.7
Peel Adhesion, 90°/SS, N/25mm	12.7	16.0	16.6
Shear, 0.5kg, minutes	129	190	237
Thickness, mm	0.67	0.75	0.70
Static Absorption, gm/sq.m./24hr	6265	3789	4648
Cold Flow, % increase/24hr/10kg	0.8	4.7	3.5
Integrity, %, 24hr.	50	78	74

Example 9

This example illustrates the preparation of a self adhesive acne pad using the teachings of the invention. The self adhesive pad contains a complex of β-cyclodextrin containing 10wt% tea tree oil, and available as EPICUTIN-TT

from Chemisches Laboratorium Dr. Kurt Richter GmbH, Berlin, Germany. This complex, although containing 10wt% tea tree oil, had no odour of the essential oil, which is liberated only by moisture.

Salicylic acid (20.0 gm) was added to polyethylene glycol PEG400 (40.0 gm) in a 100ml. screw capped bottle. The PEG400 is available from Clariant GmbH. The bottle was shaken overnight on an automatic shaker and most of the salicylic acid dissolved to make a viscous suspension.

Separately, a hot melt adhesive was prepared from Kraton KD-1161N, plasticised with a styrene-isoprene liquid rubber, LVSI-101. The Kraton KD-1161N is a blend of linear styrene/isoprene/styrene triblock copolymer and linear styrene/isoprene diblock copolymer. This material is available from Shell Chemical Company and has a bound styrene content of about 15% and a diblock content of 17%. The LVSI-101 is a block copolymer of styrene and isoprene having a styrene content of about 13% and an isoprene content of about 87%, a glass transition of about -60°C, a melt viscosity of about 2400 poises at 50°C and which is commercially available from Shell Chemical Company. Irganox 1010, a hindered phenolic antioxidant manufactured by Ciba, was used to stabilise the hot melt adhesive against thermal degradation during manufacture.

From the details given in PCT Application No: GB98/02069 the following procedure was followed. A Z-blade mixer was purged with nitrogen gas and heated to 160°C. The speed of the front, faster blade was 30 rpm. Kraton KD-1161N (100gm) and Irganox 1010 stabiliser (4.0gm) were charged to the mixer at 160°C, and the mixer was started. After mixing for 5 minutes,

the rubbery crumb coalesed, and 50gm of liquid rubber styrene-isoprene copolymer, LVSI-101, was added with continued mixing and nitrogen purging. After a further ten minutes, the temperature was raised to 170°C and the mixer front blade speed increased to 47rpm. The LVSI-101 had at this point completely mixed with the rubber, and a further 50gm of LVSI-101 was added. Ten minutes later, after blending of the second portion of the LVSI-101, a further 49gm of LVSI-101 was added, and mixed for a further 10 minutes. In this way, approximately 50gm portions of the charge of LVSI were added every 10 minutes until a total of 400gm of LVSI-101 had been added. After a further 15 minutes, the intermediate adhesive was dumped from the mixer. The total time for this operation was about 90 minutes.

Formula 2-18A	Gm.
LVSI-101	400
Kraton KD-1161N	100
Irganox 1010	4

From this intermediate mixture, referred to as Formula No 2-18A in the Tables, a finished hydrocolloid adhesive was made having the formula shown below. The Pectin USP100, NaCMC Blanose and the Vistanex polyisobutylene were mixed in the Z-blade mixer at 80°C. and the intermediate adhesive 2-18A was added at 100°C. The mixer was then cooled back to 80°C and the suspension of salicylic acid in PEG400 was added. After further mixing for 15 minutes, the mixer was cooled to 60°C, and the Epicutin-TT was added with additional mixing for 15 minutes, prior to dumping the adhesive.

Example 9	Gm.
2-18A	182.35
Vistanex LMMH	72.95
Pectin USP100	35.35
NaCMC, Blanose	35.35
PEG400	16.00
Salicylic Acid	8.00
Epicutin-TT	50.00
Total Weight	400.00

The adhesive thus contained 2.00wt% salicylic acid and 1.25wt% of tea tree oil. The adhesive was pressed between two sheets of silicone release paper in a hydraulic press at 90°C. After removing one protective silicone release paper, the sheet of adhesive was laminated to a non woven fabric, previously transfer coated with a medical grade acrylic adhesive which acts as a tie coat to bond the hydrocolloid adhesive to the fabric. Discs of the construction, 2cm in diameter, were cut. Four of the adhesive discs were applied over five days to an acne lesion on the back of a 41-year-old Caucasian female with a long history of pre-menstrual acne outbreaks. The following observations were made:

Day	No. of Disc	Adhesion level	Condition of intact skin under disc after removal	Assessment of acne after removal of disc
Day 0	-	-	-	Painful raised pimple (initial assessment)
Day 1	Disc 1	Excellent	No sign of skin redness	Pimple redness reduced, Small comedone visible
Day 2	Disc 2	Excellent	No sign of skin redness	Raised pimple reduced
Day 3	Disc 2	Excellent	(Disc left for 48 hrs)	-
Day 4	Disc 3	Excellent	Very slight sign of skin redness	Drying of lesion, comedone disappeared
Day 5	Disc 4	Excellent	No sign of skin redness	Further drying of lesion

There was a significant visual improvement over the five days in the healing of the treated acne lesion compared to an untreated lesion on the same patient. The patient found that the discs had excellent adhesion to skin. The disc, even though covered by clothing, never became adhered at its edges to the clothing, demonstrating the excellent cold flow performance of this adhesive patch. The patch gave satisfactory control of acne lesions during the peri-menstrual time.

Examples 10 - 12

These examples demonstrate the odour absorbing properties of adhesives made according to the teachings herein. An adhesive, Example 10 to be used as a control in the following experiments and containing no cyclodextrins, was made according to our copending Application number PCT No: GB98/02809 and Examples 11 and 12 were made according to the teachings herein. The compositions of the three adhesives are given in the Table below:

Amount in Mix, wt%	Example 10	Example 11	Example 12
Kraton D-1161NS	11.3	11.3	5.9
Adtac LV-E	6.0	6.0	-
Escorez 2203 LC	12.5	12.5	-
Irgafos 168	0.14	0.14	-
Irganox 565	0.07	0.07	-
Vistanex LMMH	28	28	28
LVSI 101	-	-	23.7
Irganox 1010	-	-	0.4
Cavitron 82000	-	14	-
β-Cyclodextrin W7	-	-	14
Methyl substituted β-Cyclodextrin W7M1.8	-	-	14
Sodium CMC	14	14	-
Pectin USP100	14	14	-
Aquasorb A-500	14	-	14

The three adhesives were pressed to a thickness of about 1mm between two pieces of release paper using a hydraulic press held at 90°C. The sheets were then laminated to 25μ polyurethane film, previously coated with a medical grade acrylic adhesive to act as a tie coat between the film and the hydrocolloid adhesive.

Using the MVT cups described above under the Section "Test methods - Static absorption of hydrocolloids", the pressed and laminated samples from Examples 10 - 12 were adhered to the flanges of cups that contained 30 ml aqueous NaCl solution (0.9%wt). Exactly as described in the Test method, the cups were turned upside down, put in the oven at 37°C. for 24 hours and then cooled down. The hydrocolloids were removed from the cups, the circular saline-saturated portions were cut out from the remainder of the hydrocolloid pad, and each circle was

placed in the bottom of a wide-mouthed screw-capped 1l. jar, hydrocolloid side up.

Each of the saline soaked pads was inoculated with 5µl of n-butyric acid using a microsyringe, and the caps screwed tightly on the jars. The n-butyric acid is a strong smelling compound found, together with other fatty acids, in odiferous wounds. After 24 hours, the three samples were smelled in turn by four panelists, who rated each of the three samples according to intensity of odour.

First, the panelists smelled each jar and ranked them according to strength of odour, from strongest odour to weakest. The panelists then smelled each jar a second time, and scored each on a scale of 0-5, 0 being no smell and 5 being the strongest.

These ratings of 0-5 for each adhesive were then rank ordered among the adhesives for each panelist, and the rankings for each adhesive were summed among the panelists. The following data were obtained, where 12 is the maximum possible score (highest odour), and 4 is the lowest possible score (lowest odour).

Sample	Odour Level, Sum of Rankings, Σ
Example 10	12
Example 12	7
Example 11	5

The data showed that little or no odour of n-butyric acid was detected with the adhesives of Examples 11 and 12, while the adhesive from Example 10, which contains no cyclodextrin

material, retained the strong, unpleasant odour of n-butyric acid after 24 hours.

Example 13

This example shows the incorporation of cyclodextrins into a pressure sensitive adhesive formed from a hydrogel.

A glass vessel of 250ml capacity is tared on an electronic balance and polyvinyl alcohol (0.1gm) is added, followed by 5ml of deionised water. γ-cyclodextrin (0.5gm) and α-cyclodextrin (0.5gm) are then added and the mixture is stirred vigorously until all the solid materials are dissolved. The following monomers are then introduced into the glass vessel: N,Ndimethyl acrylamide (10gm), methoxypolyethylene glycol methacrylate (MW400, 1gm), polyethylene glycol dimethacrylate (0.10gm), Daracure 1173 (CIBA, 0.4gm) and 1:2 propylene glycol (1gm).

The ingredients are mixed thoroughly and coated in a thin layer on to a piece of silicone release paper. The coated paper is passed 12 times beneath a FUSION F300S UV curing apparatus on a conveyor belt running at a speed of about 4m/min. The bulb used is 15cm long and emits light of wavelength λ in the range 200 - 400nm.

A self-supporting sheet of aqueous tacky gel is produced, which is flexible enough to be removed from the release paper, and which shows good adhesion to dry skin.

CLAIMS:

1. A pressure sensitive adhesive composition comprising a rubbery continuous phase with a discontinuous phase distributed therein, characterised in that the discontinuous phase comprises a cyclodextrin in an amount of 0.1 to 65 wt %, based on the total composition.

2. An adhesive composition according to claim 1 wherein the discontinuous phase also comprises a hydrocolloid other than cyclodextrin.

3. An adhesive composition according to claim 1 or 2 wherein the cyclodextrin is present in an amount of at least 5 wt % based on the total composition.

4. An adhesive composition according to claim 3 wherein the cyclodextrin is present in an amount of at least 10 wt % based on the total composition.

5. An adhesive composition according to any preceding claim wherein the continuous phase comprises up to 50 wt.% of polyisobutylene as a major component.

6. An adhesive composition according to any preceding claim wherein the continuous phase contains up to 15 wt.% of a rubbery copolymer of styrene or a substituted styrene as a major component.

7. A pressure sensitive adhesive composition comprising an aqueous hydrogel, characterised in that the adhesive also contains a cyclodextrin in an amount of 0.1 to 65 wt %, based on the total composition.

8. An adhesive composition according to any preceding claim which additionally contains an active ingredient.

9. An adhesive composition according to claim 8 wherein the active ingredient is complexed with the cyclodextrin.

10. An adhesive composition according to claim 8 or 9 wherein the active ingredient is selected from hydroquinone, menthol, salicylic acid, antibacterial agents, antifungal agents, essential oils and fragrances.

11. A medical or surgical appliance comprising a substrate on which is formed a layer of a pressure- sensitive adhesive composition according to any preceding claim.

12. An appliance according to claim 11 in the form of a wound dressing.

13. An appliance according to claim 11 which comprises a skin barrier.

14. An appliance according to claim 13 in the form of an ostomy appliance.

15. An appliance according to claim 13 in the form of a transdermal delivery patch for an active ingredient.

16. An appliance according to any one of claims 11 to 15 wherein the substrate includes a backing comprising non-adhesive waterproof film.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 May 2001 (04.05.01)	
International application No. PCT/GB00/02895	**Applicant's or agent's file reference** SB/OW/34876
International filing date (day/month/year) 27 July 2000 (27.07.00)	**Priority date** (day/month/year) 25 August 1999 (25.08.99)
Applicant LIPMAN, Roger, David, Arnold	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   23 March 2001 (23.03.01)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia TEFY

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
SB/OW/34876		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/ 02895	27/07/2000	25/08/1999
Applicant		
AVERY DENNISON CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. --

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BANKES, Stephen Charles Digby
BARON & WARREN
18 South End, Kensington
London W8 5BU
GRANDE BRETAGNE

SB

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ARW			DJ			ACC	
SCOB			TM's				
COMP. DIARY No.							

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)* 20.11.2001

Applicant's or agent's file reference
sb:ja:34876

IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02895	27/07/2000	25/08/1999

Applicant
AVERY DENNISON CORPORATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Senkel, H Tel.+49 89 2399-8071

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

REC'D 22 NOV 2001
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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
sb:ja:34876		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02895	27/07/2000	25/08/1999
International Patent Classification (IPC) or national classification and IPC A61L15/58		
Applicant AVERY DENNISON CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/03/2001	20.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Domingues, H Telephone No. +49 89 2399 7810

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02895

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-33	as originally filed				

Claims, No.:

1-15	as received on	02/11/2001	with letter of	02/11/2001	

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-25 (please see observations on separate sheet)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

1. Concerning section VIII

Lack of clarity in the description, Art. 5 PCT

There is an inconsistency between the discontinuous phase defined in **claim 1** and that described on pg. 13 of the description. Said phase, as defined in claim 1, comprises a cyclodextrin in an amount of 0.1 to 65 % wt %, based on the total composition and a hydrocolloid other than cyclodextrin. Although support (Art. 6 PCT) for said discontinuous phase can be found on pg. 3 of the description, on pg. 13, it is stated that *"A hydrocolloid in addition to cyclodextrin may be used in an amount from 0 wt% to 60 wt% or more,* ***and when combined with the cyclodextrin component the aggregate of the two will amount to from 0.1 wt% to 65 wt%.***". The description of the present application thus seems to provide two inconsistent definitions of one of the essential parts of the claimed pressure sensitive adhesive (the discontinuous phase) contrary to the requirements of Art. 5 PCT.

2. Concerning section V

The examination is based on the following prior art documents cited in the international search report:

D1: DATABASE WPI Section Ch, Week 198419 Derwent Publications Ltd., London, GB; Class A96, AN 1984-117671 XP002149919 & JP 59 055825 A (NITTO ELECTRIC IND CO), 31 March 1984 (1984-03-31)

D2: DATABASE WPI Section Ch, Week 199136 Derwent Publications Ltd., London, GB; Class A81, AN 1991-262350 XP002149920 & JP 03 170575 A (SEKISUI CHEM IND CO LTD) , 24 July 1991 (1991-07-24)

D3: DATABASE WPI Section Ch, Week 198333 Derwent Publications Ltd., London, GB; Class A96, AN 1983-737343 XP002149921 & JP 58 113275 A (NICHIBAN KK), 6 July 1983 (1983-07-06)

D4: DATABASE WPI Section Ch, Week 199427 Derwent Publications Ltd., London, GB; Class A92, AN 1994-222253 XP002149922 & JP 06 158002 A (SEKISUI PLASTICS CO LTD) , 7 June 1994 (1994-06-07) cited in the application

D5: DATABASE WPI Section Ch, Week 198145 Derwent Publications Ltd., London, GB; Class A96, AN 1981-82783D XP002149923 & JP 56 123912 A (NITTO ELECTRIC IND CO), 29 September 1981 (1981-09-29)

D6: PATENT ABSTRACTS OF JAPAN vol. 012, no. 344 (C-528), 16 September 1988 (1988-09-16) & JP 63 101316 A (NICHIBAN CO LTD), 6 May 1988 (1988-05-06)

D7: WO 97 39742 A (KREILGAARD BO ;HOECK ULLA (DK); KRISTENSEN HELLE (DK);

PHARMACIA &) 30 October 1997 (1997-10-30)

i) Novelty (Art. 33(2) PCT) and inventive step (Art. 33(3) PCT)

Although **D2-D6** are abstracts and therefore only contain limited information, they seem to be very relevant for the assessment of novelty and inventive step of the present application. The Applicant should bear in mind that the full documents might contain disclosures that are novelty destroying or that might preclude the recognition of inventive step.

D2 refers to a rubber tacky adhesive comprising a thermoplastic polymer, tackifier resin and cyclodextrin as deodorant. This type of adhesive can be used in food industry in order to remove offensive odours. An example is provided in which the amount of α-cyclodextrin is 1.2 wt%. **D5** discloses a pressure sensitive adhesive composition comprising pharmaceuticals, such as coronary vasodilatators complexed with a clathrating agent, for example with cyclodextrin. The amount of clathrating agent is said to be between 3-50 %.

D3 discloses pressure sensitive adhesive compositions containing pharmaceutical substances in the form of clathrate cyclodextrin (β and γ) complexes. This adhesive compositions are said to have good stability, high pharmacological action and to be suitable for use in the manufacture of adhesive tape for medical use. **D4** describes an antibacterial tape comprising a base sheet and, on one or both of the base sheets, a self adhesive layer containing an antifungal agent (thio cyanuric acid ester) clathrated with cyclodextrin. Pressure sensitive adhesives comprising oil-soluble (hydrophobic) physiologically active substances complexed with cyclodextrin are also described in **D6.** These adhesives can be applied to the skin and are said to have excellent retainability and slow releasing properties. **D7** describes the transdermal delivery of dextromethorphan, an antitussive drug, by using a drug-in-adhesive type of system in which the antitussive agent is complexed with cyclodextrin (see example 5; pg. 19, line 14-20; claims 2 and 6).

In light of the above, attention is drawn to the fact that **claims 1, 6-8 and 10** could be found to lack novelty in view of the disclosures in **D2 and D5.** Even if novelty could be established for these claims, they would still appear to lack inventive step.

From the above, it is clear that the prior art discloses pressure sensitive adhesive compositions comprising a discontinuous phase containing cyclodextrin within the range of claims 1 and 6, and an active ingredient which, in D5 and D3, is complexed with cyclodextrin. From the description, hydrocolloids, particularly hydrogels, seem to be

widely used in pressure sensitive adhesives (pgs. 1, 6 and 12-13). The person skilled in the art, when faced with the problem of providing a pressure sensitive composition according to claims 1 and 6, containing an active agent possibly complexed with cyclodextrin, would combine the information in e. g. D3 and D5 with knowledge common in the art and arrive at the subject-matter of **claims 1-4, 6-8 and 10** without the need of inventive skill.

Furthermore, it should be borne in mind that in the examples provided in the description, the amount of cyclodextrin seems to be between 14 % (examples 7, 8 and 12) and 50 % (example 4). However, the adhesive composition of example 4 showed poor static absorption. It thus seems that suitable amounts of cyclodextrin would be between 14 % and 20 % (example 2 and 3). In examples 7 and 8, which describe the use of cyclodextrin together with a carboxycelluose derivative in a hydrocolloid formulation suitable for wound dressing, the amount of cyclodextin used is 14 %. In view of this, the technical problem does not appear to be solved over the entire scope **of claims 1 and 6**.

Claim 9 does not appear inventive because adhesive compositions falling within the scope of this claim, have already been described in **D4** (see above).

Claims 11-15. From the prior art described above, it seems that pressure sensitive adhesive compositions described in the present application can have diverse uses in the delivery of different active agents. Therefore, it would be obvious to the man skilled in the art, that said adhesive compositions would be suitable for wound dressing or as an ostomy appliance (they could for example deliver an antibacterial or and antifungal agent, as described in D4). The inclusion of a skin barrier (e.g. of the hydrocolloid type) or of a backing comprising a non-adhesive waterproof film are common knowledge in the art and cannot be considered inventive.

1. Concerning section VIII

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D1: DATABASE WPI Section Ch, Week 198419 Derwent Publications Ltd., London, GB; Class A96, AN 1984-117671 XP002149919 & JP 59 055825 A (NITTO ELECTRIC IND CO), 31 March 1984 (1984-03-31)

D2: DATABASE WPI Section Ch, Week 199136 Derwent Publications Ltd., London, GB; Class A81, AN 1991-262350 XP002149920 & JP 03 170575 A (SEKISUI CHEM IND CO LTD) , 24 July 1991 (1991-07-24)

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From the above, it is clear that the prior art discloses pressure sensitive adhesive compositions comprising a discontinuous phase containing cyclodextrin within the range of claims 1 and 6, and an active ingredient which, in D5 and D3, is complexed with cyclodextrin. From the description, hydrocolloids, particularly hydrogels, seem to be

widely used in pressure sensitive adhesives (pgs. 1, 6 and 12-13). The person skilled in the art, when faced with the problem of providing a pressure sensitive composition according to claims 1 and 6, containing an active agent possibly complexed with cyclodextrin, would combine the information in e. g. D3 and D5 with knowledge common in the art and arrive at the subject-matter of **claims 1-4, 6-8 and 10** without the need of inventive skill.

Furthermore, it should be borne in mind that in the examples provided in the description, the amount of cyclodextrin seems to be between 14 % (examples 7, 8 and 12) and 50 % (example 4). However, the adhesive composition of example 4 showed poor static absorption. It thus seems that suitable amounts of cyclodextrin would be between 14 % and 20 % (example 2 and 3). In examples 7 and 8, which describe the use of cyclodextrin together with a carboxycelluose derivative in a hydrocolloid formulation suitable for wound dressing, the amount of cyclodextin used is 14 %. In view of this, the technical problem does not appear to be solved over the entire scope **of claims 1 and 6**.

Claim 9 does not appear inventive because adhesive compositions falling within the scope of this claim, have already been described in **D4** (see above).

Claims 11-15. From the prior art described above, it seems that pressure sensitive adhesive compositions described in the present application can have diverse uses in the delivery of different active agents. Therefore, it would be obvious to the man skilled in the art, that said adhesive compositions would be suitable for wound dressing or as an ostomy appliance (they could for example deliver an antibacterial or and antifungal agent, as described in D4). The inclusion of a skin barrier (e.g. of the hydrocolloid type) or of a backing comprising a non-adhesive waterproof film are common knowledge in the art and cannot be considered inventive.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02895

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L15/58 A61L24/00 A61L24/08 A61L26/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 198419 Derwent Publications Ltd., London, GB; Class A96, AN 1984-117671 XP002149919 & JP 59 055825 A (NITTO ELECTRIC IND CO), 31 March 1984 (1984-03-31) abstract ---	1-4, 6-13,15
X	PATENT ABSTRACTS OF JAPAN vol. 012, no. 344 (C-528), 16 September 1988 (1988-09-16) & JP 63 101316 A (NICHIBAN CO LTD), 6 May 1988 (1988-05-06) abstract --- -/--	1,2, 7-13,15

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 October 2000	24/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Thornton, S

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 39742 A (KREILGAARD BO ;HOECK ULLA (DK); KRISTENSEN HELLE (DK); PHARMACIA &) 30 October 1997 (1997-10-30) example 5 claims 1,2,6 ---	1,5, 8-11,13, 15
X	DATABASE WPI Section Ch, Week 199136 Derwent Publications Ltd., London, GB; Class A81, AN 1991-262350 XP002149920 & JP 03 170575 A (SEKISUI CHEM IND CO LTD) , 24 July 1991 (1991-07-24) abstract ---	1,6
X	DATABASE WPI Section Ch, Week 198333 Derwent Publications Ltd., London, GB; Class A96, AN 1983-737343 XP002149921 & JP 58 113275 A (NICHIBAN KK), 6 July 1983 (1983-07-06) abstract ---	1,8-11
X	DATABASE WPI Section Ch, Week 199427 Derwent Publications Ltd., London, GB; Class A92, AN 1994-222253 XP002149922 & JP 06 158002 A (SEKISUI PLASTICS CO LTD) , 7 June 1994 (1994-06-07) cited in the application abstract ---	1,8-11
X	DATABASE WPI Section Ch, Week 198145 Derwent Publications Ltd., London, GB; Class A96, AN 1981-82783D XP002149923 & JP 56 123912 A (NITTO ELECTRIC IND CO), 29 September 1981 (1981-09-29) abstract -----	1,8-11

INTERNATIONAL SEARCH REPORT

...on patent family members

Inte...al Application No
PCT/GB 00/02895

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 59055825 A	31-03-1984	JP 1331151 C	14-08-1986
		JP 60056687 B	11-12-1985
JP 63101316 A	06-05-1988	NONE	
WO 9739742 A	30-10-1997	AU 714942 B	13-01-2000
		AU 2313297 A	12-11-1997
		CA 2251966 A	30-10-1997
		EP 0904067 A	31-03-1999
		JP 2000509037 T	18-07-2000
JP 3170575 A	24-07-1991	NONE	
JP 58113275 A	06-07-1983	JP 1593077 C	14-12-1990
		JP 2016289 B	16-04-1990
JP 6158002 A	07-06-1994	NONE	
JP 56123912 A	29-09-1981	JP 1625236 C	18-11-1991
		JP 2040645 B	12-09-1990

CYCLODEXTRIN CONTAINING PRESSURE SENSITIVE ADHESIVES

This invention relates to pressure sensitive adhesive compositions containing cyclodextrins. By the term "pressure sensitive adhesive" is meant those adhesives that have touch perceivable tack, that are easily deformed in the time scale allowed for bond formation and that are capable of being applied and bonded to the substrate at temperatures no higher than about 50°C, and preferably at ambient temperatures. Pressure sensitive adhesives are employed in many fields. Pressure sensitive adhesives are used, *inter alia*, as components of labels, industrial tapes, postage stamps, stationery products, and in medical products such as surgical drapes, tapes, ostomy products, wound care products and devices for transdermal drug delivery.

This invention relates particularly to pressure sensitive adhesives used in contact with skin and more particularly to the class of medical pressure sensitive adhesives that are generally termed hydrocolloid adhesives. Most particularly, the invention relates to adhesives that are able to absorb odours associated with body fluids and/or wounds, and to adhesives that have improved ability to deliver active ingredients to wounds or skin.

Hydrocolloid adhesives are a unique kind of medically useful pressure sensitive adhesive. They have usually two phases - a rubbery phase which provides pressure sensitive tack, sometimes called "dry tack" and, dispersed within the continuous rubbery phase, a discontinuous phase of absorbent material. Depending upon the nature of the absorbents, and especially whether the absorbent is soluble in aqueous media or merely swellable, the adhesive composition can develop "wet

tack" as it becomes imbibed with fluid. Such wet tack can also influence the adhesive power of the hydrocolloid. Hydrocolloid adhesives thus have a duality of attributes in that they are inherently adhesive and inherently absorbent. They are useful as wound dressings because they can be applied directly to open wounds and can be secured on the surrounding intact skin, and as skin barriers because they protect the peristomal skin of ostomy patients. Hydrocolloid adhesives maintain the skin in a normally or optimally hydrated condition. Optimally hydrated skin is less subject to irritation and injury from repeated application and removal of adhesives than is macerated skin, which latter can result from the use of conventional pressure sensitive adhesives on the skin.

Many hydrocolloid skin barriers are known and are used especially in the fields of ostomy care and wound care. It is convenient to divide these into "integrated" compositions and "non-integrated" compositions. In this context, "integrated" means those compositions that substantially retain their dimensional stability and form when saturated with wound exudate and/or other body fluid. Integrated hydrocolloids usually contain cross-linked or pseudo cross-linked rubbery matrices in the continuous phase to provide the integrating network. But specific combinations of absorbents have also been reported to give highly integrated hydrocolloids, even in the absence of a cross-linked rubbery matrix. "Non-integrated" means those compositions which become soft gels and amorphous as they become saturated with fluid. In this invention, both integrated and non-integrated hydrocolloids are encompassed.

It is often desired to add small quantities of an agent to a medical pressure sensitive adhesive to confer additional benefits. For example, skin problems are common for persons

who have a stoma, which is an artificial body opening produced as a result of surgery. PCT Application WO 98/01167 discloses in this regard a hydrocolloid pressure sensitive adhesive containing an amount of aloe vera up to 5wt% which is said to offer a better protection of the skin against the aggressive action of excreted substances. Again, in European Patent Specification No. 0 023 395 B1, mention is made of pressure sensitive adhesives containing a broad spectrum antimicrobial agent. In this prior art, the antimicrobial agent is dissolved in a suitable solvent and dispersed in the said pressure sensitive adhesive to give a two-phase system, which is said to release the antimicrobial agent in a controlled way.

If the context permits, we use in this Application the term "hydrocolloid" to embrace the term "cyclodextrin", and within the scope of the invention a cyclodextrin may be or may not be the only hydrocolloid present in the adhesive.

According to a first aspect of the present invention there is provided a pressure sensitive adhesive composition comprising a rubbery continuous phase and a discontinuous phase, wherein the discontinuous phase comprises 0.1 to 65 wt%, preferably at least 5 wt% of a cyclodextrin material, and optionally a hydrocolloid other than a cyclodextrin, said percentages being based on the total composition. The preferred minimum of cyclodextrin in a composition according to this aspect of the invention is 10 wt%. The discontinuous phase in total preferably comprises 5 to 70wt% of the total composition, more preferably 10 to 60wt%.

A further aspect of the present invention relates to constructions comprising a layer of cyclodextrin containing hydrocolloid adhesive that further contains an effective

amount of one or more active ingredients. Hydrocolloid adhesives are particularly suitable as the basis for such constructions, because of their ability to maintain the skin in a normally or optimally hydrated condition. Often, such skin patches will be applied to the skin over an extended period, and hydrocolloid adhesives will maintain the skin in a healthy condition. As non-limiting examples of what is contemplated, the active ingredient may be an antibacterial or antifungal compound, a compound such as hydroquinone, a compound such as an essential oil, for example tea tree oil, or mixtures of essential oils, a compound such as salicylic acid, a compound such as menthol, or a fragrance composition. Hydrocolloid adhesives containing such active ingredients can be made into, for example, skin patches that will deliver the active ingredient to the skin surface. The advantage of using cyclodextrin complexes of these active ingredients is that often the active ingredients are labile, or not soluble, or not stable, or may interact with other ingredients in the formulation. Inclusion of these active ingredients within the molecular structure of the cyclodextrins provides an effective way of insuring delivery to the target skin site. It will be understood that, within the scope of the invention, the active ingredient does not have to be complexed within the cyclodextrin molecule - it can also be present in a free, or uncomplexed, state. The cyclodextrin will function in such cases as odour absorbing means, and/or as absorbing means. In the case of compositions containing more than one active ingredient, again the complexing of one or more of the active ingredients within a cyclodextrin molecule is optional.

Complexing is a preferred feature however, and according to a further aspect of the invention there is provided a pressure sensitive adhesive composition containing 1 to 10 wt%

of cyclodextrin, all or part of which is complexed with one or more active ingredients of this composition.

Non-limiting examples of prior art hydrocolloid compositions suitable for use as bases for the reduction to practise of the present invention, with appropriate modification in accord with the teachings herein described, are given in US Patent 3,339,546, US Patent 4,231,369, US Patent 4,477,325, US Patent 4,738,257, US Patent 4,551,490, US Patent 4,192,785, US Patent 4,952,618, all of which patents are incorporated herein by reference.

The present invention also provides skin barriers and wound dressings comprising a layer of hydrocolloid adhesive containing an effective amount of a cyclodextrin and which is backed by a non-adhesive, waterproof film to form a skin barrier or dressing. The skin barrier is used in a number of ways. One of these is for wound dressing purposes. Patients in institutional settings such as hospitals and nursing homes often have or acquire chronic wounds such as venostasis ulcers and bed sores, and these wounds can possess a very offensive odour. Bandages or dressings made from or incorporating the compositions of the invention are able to absorb odour molecules and thereby reduce or eliminate the offensive odour. This contributes to the well-being of the patient as well as to the nursing staff and other patients, since the odours from chronic wounds can be offensive to both carers and to family members of the patient. Another important use is for the protection of the skin around body openings, especially around the surgically created openings known as colostomies, ileostomies and urostomies. Collectively, these surgically created body openings are often termed stomas. The novel skin barriers of the invention are able to absorb the odour

molecules that are associated with faeces and urine and thus are able to assist in the control of the odour that is associated with stomas. This can increase the self-confidence of the patient because such odours can be a source of personal embarrassment. While not wishing to be bound by any particular theory, it is believed that the cyclodextrin molecules are able to absorb malodorous molecules, which become complexed within the toroidal structure of the cyclodextrin molecule.

One yet further aspect of the invention relates to incorporation of cyclodextrin materials into pressure sensitive adhesives based on hydrophilic polymers, which will usually, though not necessarily, be crosslinked. These materials are commonly termed hydrogels, and can form the basis of medical pressure sensitive adhesives. With hydrogels, the pressure sensitive adhesive property is achieved by plasticisation of the polymer with water and/or a hydrophilic plasticiser, and thus the cyclodextrin may or may not be completely dissolved in the pressure sensitive adhesive, depending on whether the cyclodextrin is completely soluble in the plasticising medium. Thus, the possibility exists with this adhesive system for a cyclodextrin containing pressure sensitive adhesive that has only one phase.

Adhesives containing fragrance compositions are very useful to mask the bad odours associated with the presence of urine and faeces on the skin, which can occur with ostomy patients. Often, fragrances can be irritating to the skin, or can cause allergic reactions. When the fragrances are first complexed with a cyclodextrin material, the fragrance is released when the cyclodextrin becomes moist, and the amount liberated is controlled by the rate and amount of moisture ingress. In this way, any irritation potential or allergic

response with the particular fragrance is minimised or eliminated.

The introduction of cyclodextrins, in combination with certain "active compounds", into pressure sensitive adhesives is known and is reported in the prior art.

For example Japanese Patent Application JP 6158002A, to Sekisui Plastics Co., describes an antibacterial pressure sensitive adhesive for food containers, wherein isothiocyanuric acid ester is complexed within β-cyclodextrin and added to a pressure sensitive adhesive which is then adhered to the inside surface of the food container to control bacterial and fungal growth.

US Patent 5,352,717 to American Maize Technology Inc. teaches adhesive or sealant compositions containing a small amount of cyclodextrin. Some examples also have, as an optional component, a blowing agent to expand the adhesive to a foamed material for industrial uses. Although one of the examples talks to a "pressure sensitive adhesive", the exemplified adhesive is said to be applied at temperatures of 160°C., as are the other examples, which are clearly directed at hot melt adhesive compositions, outside the contemplated area of interest of the instant invention.

US Patent 4,978,532 to Pharmedic Co. describes a dosage form for the administration of dehydroepiandrosterone (DHEA). The dosage form comprises a medical grade silicone pressure sensitive adhesive, DHEA and a permeation enhancer, an example of which is hydroxypropyl-β-cyclodextrin.

Also of interest is the US Patent 5,562,917 to Pentech Pharm Inc. that claims a composition suitable for the treatment of Parkinson's disease involving the transdermal delivery of apomorphine in an aqueous based gel. Specified is a permeation enhancer which includes hydroxypropyl-β-cyclodextrin. Also specified is a matrix of silicone copolymer pressure sensitive adhesive, 0.1 - 3wt% of apomorphine and a carbocyclic compound having pendant hydroxyl groups selected from butylated hydroxy anisole, butylated hydroxy toluene and hydroxypropyl-β-cyclodextrin as a permeation enhancer.

The use of cyclodextrins in cosmetics as odour absorbing agents and as vehicles to deliver active ingredients to, for example, the skin, is known in the literature. For example, PCT Applications WO 98/56343 WO 98/56344 and WO 98/56345 disclose cosmetic compositions for topical application to the skin that contain an aqueous phase or a water-in-silicone emulsion, a cyclodextrin compound and a salicylic acid derivative. Such compositions are said to provide anti-acne and anti-inflammatory activity together with reduced skin irritation.

PCT Application WO 99/06078 discloses cyclodextrin odour absorbent articles for decreasing odours associated with body fluids, where the cyclodextrin has a specific particle size. PCT Application WO 98/56890 teaches the combination of aqueous cyclodextrin compositions with wrinkle control agents for odour and wrinkle control of fabrics. PCT Applications WO 98/17239, WO 98/17240, WO 98/56341 and WO 98/56342 describe an aqueous carrier containing soluble cyclodextrins, perfume compositions and preferably hydrophobic antimicrobial compounds in order to reduce body odour and or environmental odour. PCT Applications WO 98/18439 and WO98/56340 reveal

similar compositions in a powder carrier such as a starch. PCT Application WO 98/56339 describes similar compositions in a two phase formulation comprised of an aqueous phase and an oil phase.

US Patent 5,429,628 and PCT Application WO 94/22501 both teach the preparation of articles containing small particle size cyclodextrin for odour control. A large number of consumer absorbent products, such as panty liners, catamenials, diapers and sanitary napkins are exemplified, where the cyclodextrin is present within, or as part of, a fibrous absorbent medium.

European Patent Specification 0 392 608 B1 concerns solid consumer product compositions containing an ingredient such as a flavour, a drug or a perfume that is complexed within a cyclodextrin. Product categories that are mentioned include those such as drinks and beverages, canned pet foods, cosmetics and toiletries such as facial scrubs, body powders, depilatories, mouth washes and lipsticks, detergents, paper towels, cake mixes and cookies, incense, room deodorant blocks, dyes, insect repellents and the like.

PCT Patent Application WO 94/18973 discloses the complexing of bisacodyl with cyclodextrin to provide an oral dosage form that delays the laxative action of the bisacodyl until the preparation is near the junction of the small intestine and the colon.

US Patent 5,246,611 and PCT Applications WO 93/05136 and WO 91/17300 all deal with the use of cyclodextrin perfume complexes in fabric treatment products such as fabric softeners. The cyclodextrin complexes are suspended in

polyalkylene glycol carrier which does not prematurely displace the active from the cyclodextrin.

What becomes evident from a reading of the prior art is that, notwithstanding the very great amount of art that exists concerning cyclodextrin containing materials, nowhere in the literature is reported the use of cyclodextrins as an integral component in pressure sensitive adhesive compositions.

Concerning odour absorbent adhesives, there appears to be little or no prior art. Japanese Application 10168348A to Kodaijin Sugaoka KK does disclose incorporation of cristobalite as a component of wall coatings which also contain pressure sensitive adhesives, and the cristobalite is said to absorb foul odours. But the finished composition is not itself pressure sensitive adhesive; indeed, it is said to resemble Japanese lime plaster.

McNeil-PPC Inc. in US Application 93168550 A disclose panty liners in which a pressure sensitive adhesive is applied to an absorbent structure containing baking soda to absorb odours. Plasto SA, in German Application 19724871 A1, claim a laminated structure comprised of a polyolefin film having dispersed in it a perfume, and coated on one side with a pressure sensitive adhesive. Such a structure will obviously serve only to mask an odour, and the perfume is in the film, not in the adhesive. Schering Plough in US Patent 5,399,404 teach a patch for masking foot odours comprising a carrier on one side of a non-occlusive layer which contains fragrance and a pressure sensitive adhesive on the other side of the carrier to secure the patch to the foot or shoe. In PCT WO 9423766 A1, Schering Plough also disclose a deodoriser for masking foot and shoe odours comprised of a pressure sensitive adhesive

laminated to a felt which contains a perfume. Kock in Canadian Application 2041278 A describes a disposable perspiration absorbing pad which can be adhered to clothing and adjusted in size and shape and which contains an odour absorbing or perfumed layer.

In none of the above prior art is there any reference or suggestion that the pressure sensitive adhesive component is itself odour absorbing, or which itself delivers a perfume.

What is surprising and unexpected in the instant invention is that, if cyclodextrins are employed as the integral absorbant filler, or as part of the integral absorbent fillers, in hydrocolloid adhesives, the resulting compositions have a unique and wide versatility. They are capable of adhering to surfaces, absorbing fluids, absorbing odours, providing a fragrance and delivering active substances. There is no indication or suggestion in the literature to add or incorporate cyclodextrins into hydrocolloid adhesives, nor any indication or suggestion that such addition should yield the advantageous results of odour control and reduction. Further, is there no suggestion or indication that fragrances and many active ingredients may advantageously be delivered to the skin by incorporating them into such cyclodextrin containing hydrocolloid adhesives.

The adhesive of the invention comprises any suitable pressure sensitive adhesive matrix known in the art and having hydrocolloid particles and/or cyclodextrins dispersed or dissolved therein. The permanently tacky pressure sensitive adhesive component must be tacky at room temperature as well as at the skin temperature of patients. Also, the adhesive must be dermatologically acceptable, which means that after

continuous contact with skin there is little adhesive residue upon removal and there is no significant reaction with the skin during the adhesion period. The adhesive strength of the continuous phase must be sufficient to adhere to the skin of the patient for the time determined by the use of the medical device of which the adhesive forms part. Other ingredients such as tackifiers, plasticisers, and polymer stabilisers may be added to the continuous rubbery phase, to modify tack and optimise adhesion properties and to protect polymers from degradation during processing.

The adhesive matrix may be based on for example polyisobutylene, butyl rubber, polyacrylates, polyurethanes, silicone gum, natural gum rubber, SBR rubber or polyvinyl ether. Thermoplastic elastomers such as styrene-isoprene-styrene block copolymers and styrene-ethylene/propylene-styrene block copolymers may be used, and these may require optional tackifiers and plasticisers. Blends or mixtures of elastomers may be employed. Conventional additives such as tackifiers, softeners, plasticisers and antioxidants may be present to modify, adjust and stabilise the adhesive and other properties of the matrix. The amount of adhesive matrix with respect to the total composition will generally be from 35wt% to about 99wt% or more. Hydrophilic polymers, such as are used in hydrogels, may also form the basis of the pressure sensitive adhesive matrix.

Suitable hydrocolloids for use in the adhesives in conjunction with the cyclodextrins are naturally occurring hydrocolloids such as pectins, guar gum, karaya gum, locust bean gum, carageenan, tragacanth gum, alginates, xanthan gum, modified naturally derived substances such as sodium carboxymethyl cellulose, synthetic materials such as

polvinylalcohol, polyoxyalkylene polyols, polyvinyl pyrollidone, and animal derived materials such as gelatine. Ionic hydrocolloids such as hyaluronic acid, chitosan salts or DEAE Dextran may also be employed. The hydrocolloids may be water absorbable or water swellable, and combinations of one type or of various types may be used in any ratio. A hydrocolloid in addition to cyclodextrin may be used in an amount from 0wt% to 60wt% or more, and when combined with the cyclodextrin component the aggregate of the two will amount to from 0.1wt% to 65wt%.

The term cyclodextrin, as used herein, includes any of the known cyclodextrins. Cyclodextrin materials are cyclic oligosaccharides containing a minimum of six D-(+)-glucopyranose units attached by α- (1 > 4) glucosidic bonds. Three cyclodextrins called α, β and γ are naturally occurring and have, respectively, six, seven and eight glucose units. Cyclodextrins are known that contain up to twelve glucose units. Cyclodextrin materials can also be manufactured from starch by enzymatic degradation. In addition, many synthetic modifications of the natural material materials are known, for example methyl-β-cyclodextrin and hydroxypropyl-β-cyclodextrin. The conformations of the cyclic structures of these molecules are such that the molecules are arranged in rigid conical molecular shapes that have hollow interiors of very well defined sizes. These internal cavities are hydrophobic in nature because the interior of the toroidal shape is predominantly made up of hydrogen atoms. The interior shapes of the cyclodextrins are able to form inclusion complexes, sometimes referred to as "host-guest" complexes, or clathrate compounds, with organic molecules which fit, completely or partially, into the cavities defined by the toroidal shapes. For example, odiferous molecules can fit into

the cavities. This includes both perfumes and malodorous compounds. Cyclodextrins therefore, and especially mixtures of cyclodextrins with cavities of different sizes, can be used to control odours. With respect to odour control, there is scope for two different approaches within the present invention. First, uncomplexed or free cyclodextrins, dispersed within the adhesive matrix, can be used to absorb malodours. Second, perfumes can be precomplexed with cyclodextrins and then formulated in the final adhesive. The perfume is then released *in situ* and will mask the undesirable odour. (Once a cyclodextrin molecule has released its precomplexed perfume molecule, it is then available to complex a malodorous molecule). The complexation of odorous molecules by cyclodextrin and the release of precomplexed perfume molecules from cyclodextrin are facilitated by the presence of water. It will be understood that the water necessary to facilitate such release of perfume and complexing of malodour by the cyclodextrin is present in the contaminating urine or faeces, and/or is released by the skin through normal transpiration, and will be absorbed by the adhesive.

The choice of cyclodextrin employed in a given formulation will be decided on the basis of the properties desired in the finished product, and the specific role that the cyclodextrin is fulfilling. Unmodified β-cyclodextrin is not very water soluble and is generally not preferred if high absorbancy is needed. α-cyclodextrins, γ-cyclodextrins and certain modified β-cyclodextrins are more water absorbent. Mixtures of cyclodextrins are often preferred, because these will absorb a wider range of malodorous molecules than will a single cyclodextrin. The cyclodextrin to be used for a specific complex will of course be determined by the size and shape of the active molecule to be complexed.

Any active ingredient may be considered for addition to the formulations anticipated by the instant invention. By active ingredient, we mean an ingredient that is not essential to the functioning of the formulation as a moisture and odour absorbing pressure sensitive adhesive. An active ingredient is added to confer an additional benefit to the formulation. It is not necessary that the active ingredient first is complexed with a cyclodextrin prior to mixing into the formulation, nor indeed that it complexes with a cyclodextrin at all, although it will generally be advantageous if the active ingredient is so complexed. The following active ingredients exemplify the scope of the invention, and represent a non-limiting list of active ingredients.

Aspirin, benzocaine, benzyl alcohol, butamben picrate, camphor, camphorated metacresol, chloral hydrate, chlorabutanol, chloraxylenol, cyclomethycaine sulphate, dibucaine, dibucaine hydrochloride, dimethisoquin hydrochloride, diphenhydramine hydrochloride, dyclonine hydrochloride, eugenol, glycol salicylate, hexyl resorcinol, hydrocortisone, hydrocortisone acetate, juniper tar, lidocaine, lidocaine hydrochloride, menthol, methapyrilene hydrochloride, phenol, phenolate sodium, pramoxine hydrochloride, resorcinol, resorcinol monoacetate, salicylamide, tetracaine, tetracaine hydrochloride, thymol, triethanolamine salicylate, tripelennamine hydrochloride, allyl isothiocyanate, ammonia, capsaicin, eucalyptus oil, histamine dihydrochloride, methyl nicotinate, methyl salicylate, turpentine oil, allantoin, calamine, dimethicone, glycerin, kaoline, petrolatum, shark liver oil, zinc acetate, zinc carbonate, zinc oxide, hydroquinone, quinine sulphate, vitamine E, pregnenolone acetate, progesterone, salicylic

acid, clioquinol, haloprogin, miconazole nitrate, tolnaftate, undecylenic acid, benzoyl peroxide, sulphur, povidone iodine, benzalkonium chloride, benzethonium chloride, methylbenzethonium chloride, trichlosan, trichlocarban, chlorhexidine gluconate, bacitracin zinc, neomycin sulphate, glycolic acid, tea tree oil, lavender oil.

Active ingredients must be present at sufficient concentrations to achieve the desired effect. In general, however, active ingredients will be present usually at no greater than 10wt%, and preferably at no greater than 5wt%, with respect to the total composition.

Other components such as chemical agents that facilitate release of active ingredients from the adhesive formulations, for example plasticisers and solvents for the active ingredients be optionally be present. Also agents that promote absorption of active ingredients by the skin, may optionally be added to the formulation. Non-limiting examples of such skin permeation enhancers are isopropyl myristate, oleic acid, propylene glycol and laurocapram. Other optional ingredients such as small amounts of pigments or colourants may also be present in the compositions.

Test Methods

The formulations in the examples below were evaluated using the following test methods.

Reverse tack

Reverse tack of hydrocolloid adhesives is the maximum force necessary to remove a standard polyester strip brought into

contact with the hydrocolloid without external force, from this hydrocolloid surface.

Procedure

Make the test panel self adhesive using double coated tape. Laminate the hydrocolloid adhesive on the test panel. Place the test panel with hydrocolloid in the lower clamp of a tensile testing machine. Program the tensile tester. Place a polyester test strip of thickness 125 μ (5 mils) and dimensions (21 cm x 2.54 cm) in the upper clamp, making sure that the total length of polyester under the clamp (loop) is 15 cm. Remove the release liner from hydrocolloid and start the measurement.

The reverse tack is the maximum force to remove the polyester strip from the hydrocolloid surface.

90° Peel adhesion of hydrocolloid adhesives on SS

Peel adhesion on stainless steel (SS) is the average force to remove a hydrocolloid adhesive, laminated under specified conditions on a SS panel, from the SS panel at constant speed and at an angle of 90°.

Procedure

Clean the SS-panel with solvent. Cut a hydrocolloid sample of 25.4mm width and reinforce with reinforcing tape, laminate a paper strip at one end of the hydrocolloid sample using an overlap of about 1 cm. Remove the liner from the hydrocolloid sample and laminate the sample on the SS-panel with a 450 gm. roller at a speed of 150 cm/min. Allow the sample to dwell for 1 minute. Place the paper strip in the upper clamp and the SS-panel on the lower clamp, making sure that the angle between peel direction and SS-panel is 90°. Start the measurement

using a crosshead speed of 300mm/min. The angle must be kept 90° until the measurement is completed. The 90° peel adhesion is the average force to remove the hydrocolloid strip from the SS-panel.

Static shear of hydrocolloid adhesives

Static shear is the time necessary to remove a hydrocolloid adhesive, laminated on a stainless steel panel under specified conditions, from the test panel under influence of a specified weight.

Procedure

Condition the hydrocolloid samples at 23 ± 1° and 50 ± 2% relative humidity for 24 hours. Clean the SS shear panel with solvent. Cut a hydrocolloid strip of 25.4 mm width and 50 mm length. Reinforce the hydrocolloid strip with reinforcing tape. Laminate the hydrocolloid strip on the test panel using an overlap surface of 1 inch². Protect the free hydrocolloid with release liner. Put a weight of 500 g on the laminate for 1 hour. Reinforce the free hydrocolloid adhesive zone with reinforcing plastic and perforate. Place the test panel with hydrocolloid on the shear bar using a shear weight of 500 g. Re-zero the registration-clock. Note the time on the clock when sample falls off under the influence of the 500g. Weight. This completes the measurement.

Static absorption of hydrocolloids.

To determine the amount of fluid uptake into a known surface of hydrocolloid adhesive.

Procedure

Laminate release liner to the upper flange of a moisture vapour transmission determination cup with the double coated

tape. This is the contact zone for the hydrocolloid. Fill the cup with 30 ml NaCl solution (0.9%wt). Cut a sample of hydrocolloid of about the same size as the outer cup diameter. Weigh the sample (W_1). Laminate the sample to the cup, making sure that the seal between the hydrocolloid sample and the cup is water tight. Turn the cup upside down and put it in the oven at 37°C. for 24 hours. Cool down. Remove the hydrocolloid from the cup and reweigh (W_2). Calculate the water fluid absorption (g/sq.m.24h) using the formula :

$$abs = (W_2 - W_1) / 0.002375$$

where the area of the hydrocolloid in contact with salt solution is 0.002375 sq.m.

Determination of cold flow

The flow of the hydrocolloid under influence of a specified pressure and after a specified time, is measured.

Procedure

Condition the hydrocolloid samples at 23 ± 1°C and 50 ± 2 % relative humidity for 24 hours. Cut 5 samples of hydrocolloid using a 35mm circular die-cutter. Put a silicone paper on top of a first glass plate. Arrange the 5 samples on the silicone paper in a way that pressure is distributed equally. Measure the diameter of each sample with callipers, mark the exact place where the measurement is done. Put a plastic disk on each sample. Put another silicone paper and two glass plates over the construction followed by a weight of 10 kg. (The measurement can also be done by placing the sample with the disk and the 10kg. weight in an oven maintained at 40°C). After 24 hours, measure the diameter of the samples where they are marked. Calculate the % increase of

diameter of the samples. The cold flow is the % increase of diameter after 24 hours exposure to 10 kg (for 5 samples). Record the % increase in diameter and the test temperature.

Determination of the integrity of hydrocolloids

The integrity of a hydrocolloid is defined as its ability to resist breakdown by biological fluids. The test measures the weight percentage of hydrocolloid adhesive retained after exposure to saline under specified conditions.

Procedure

Condition the hydrocolloid samples at 23 ± 1°C and 50 ± 2 % relative humidity for 24 hours. Cut circular samples 2.54cm in diameter from hydrocolloid sheet. Weigh and record the samples (W_i). Place each sample in a bottle with 50ml aqueous saline (0.9%wt). Cap the bottles and agitate on the bottle shaker at 400 speed for a period of 18hrs. Remove the sample and dry it in the circulating air oven at 50°C and 50% relative humidity until dry. This takes about 24 hours. Weigh and record the sample (W_f). The Integrity Value of the sample is calculated using the following equation:

$$\text{Integrity Value (\%)} = 100 \times \frac{(W_f)}{(W_i)}$$

Preparation of Cyclodextrin Complexes

The preparation of cyclodextrin complexes is described in the literature, and illustrative methods are incorporated herein for reference only.

A complex of γ-cyclodextrin and triclosan was formed by allowing a suspension of triclosan in an aqueous solution of γ-cyclodextrin (molar ratio 1.25 γ-cyclodextrin: 1.0 triclosan) to equilibrate for 24 hours at 25°C. with constant stirring. At equilibrium, a dense white precipitate corresponding to a 1:1 stoichiometric ratio of γ-cyclodextrin to triclosan was formed.

A complex of citral in β-cyclodextrin was prepared by mixing 200ml water and 62gm β-cyclodextrin at room temperature. Citral (7.6gm) was added dropwise to the suspension of β-cyclodextrin. After intensive stirring at room temperature for about 10 hours, the suspension was allowed to stand for a further 24 hours. The complex was filtered and vacuum dried at 40°C.

A complex of citral in γ-cyclodextrin was prepared by dissolving 70gm γ-cyclodextrin in 200ml water at 50°C, and adding citral (7.6gm) dropwise to the γ-cyclodextrin solution. After intensive stirring at 60°C for about 6 hours, the solution was allowed to stand for a further 24 hours. The complex was filtered and vacuum dried at 40°C. The concentration of citral in the γ-cyclodextrin complex was 11wt%.

A complex of evening primrose oil in γ-cyclodextrin at a level of 15wt% oil was prepared by dissolving 70gm γ-cyclodextrin in 200ml water at 45°C, and adding the evening primrose oil dropwise to the γ-cyclodextrin solution. Stirring was continued for 6 hours, and the complex was allowed to cool

and stand for a further 24 hours, after which time it was filtered and dried *in vacuo*.

The invention will now be further described with reference to the following non-limiting examples.

Examples 1 - 4

These examples illustrate a cyclodextrin containing hydrocolloid adhesive suitable for a WC flushable ostomy pouch. This flushable requirement means that the hydrocolloid should not be integrated, so that it will disintegrate satisfactorily in the sewage system. Example 1 is a hydrocolloid containing polyisobutylene, pectin, gelatine and sodium carboxymethyl cellulose, which was made as a control material. This hydrocolloid, described in US Patent 3,339,546, is an inelastic, non-integrated hydrocolloid adhesive which has been on the market as an ostomy barrier material and as a wound dressing material for many years, and is considered a standard product.

Each formulation was prepared in a 500gm batch in a 1l. Z-blade mixer. The pectin, the sodium carboxymethyl cellulose and the third powder was added to the mixer at 90°C and the powders blended together for 2 minutes. Then the Vistanex LMMH was added to the powders and the formulations were further mixed for 30 minutes at 90°C. The finished hydrocolloid adhesives were made into sheets of approximately 1mm thickness by pressing about 130gm of each formulation between two sheets of silicone release paper in a hydraulic press at 90°C.

Wt% of Each Raw Material	Ex. 1	Ex. 2	Ex. 3	Ex. 4
Polyisobutylene, Vistanex LMMH	40.6	40.6	40.6	50.0
GenuPectin USP 100	19.8	19.8	19.8	-
Sodium CMC, Blanose 7H4XF	19.8	19.8	19.8	-
Gelatine 100 mesh, 225 Bloom	19.8	-	-	-
β-Cyclodextrin (Cavitron 82000)	-	19.8	-	-
Hydroxypropyl β-Cyclodextrin (Cavitron 82005)	-	-	19.8	50.0
Totals, wt%	100	100	100	100

Physical Data	Ex. 1	Ex. 2	Ex. 3	Ex. 4
Reverse Tack, N/25mm	17.5	21.5	20.3	18.7
Peel Adhesion, 90°/ Stainless Steel, N/25mm	8.8	7.9	12.0	15.0
Shear, 0.5kg, minutes	94	68	58	43
Thickness,mm	1.27	1.20	1.06	1.00
Static Absorption, gm/sq.m./24hr	7280	7242	7301	177
Cold Flow, % increase/24hr/10kg	7.2	18.7	11.7	18.6
Integrity, %, 6hr	65	82	58	97

Example 5

The hydrocolloid adhesive of Example 3 is laminated to a spun laced nonwoven fabric which had previously been waterproofed and coated with a medical grade acrylic pressure sensitive adhesive. The acrylic adhesive functions as a tie layer to bond the hydrocolloid adhesive to the polyester fabric. Such an acrylic adhesive coated nonwoven fabric is available commercially from Smith & Nephew plc as Lasso SA72.

The skin barrier so produced is made up into a drainable ostomy pouch having a stoma hole size of 32mm. The stoma pouch is used by a 22 year old ileostomy patient who is experiencing leakage problems with his commercially available pouch. The hydrocolloid adhesive of Example 3 has a high cold flow value, which means that the adhesive flows easily into the scarred depression on the patient's abdomen close to the stoma.

Although the hydrocolloid on the stoma erodes somewhat within 24 hours, the pouch adheres well, and the adhesive absorbs the odour caused by faecal contamination at the edge of the adhesive exposed close to the stoma opening. The patient is pleased with the performance of the pouch, and states that there is less odour noticeable with the pouch of example 5 compared to his current commercially available pouch.

Examples 6 - 8

Examples 6 - 8 show the effect of substituting cyclodextrins for one ingredient in a moderately integrated hydrocolloid formulation suitable for use as a hydrocolloid wound dressing. Aqualon A-500, which is a crystalline sodium carboxycellulose, was substituted with cyclodextrin material. 500gm batches of each formulation were prepared. The polyisobutylene (Vistanex LMMH), the Pectin, the Blanose sodium CMC and the third powder were added at 90°C to a 1l. Z-blade mixer. After mixing for 15 minutes at 90°C, the temperature was raised to 100°C, and the other ingredient, the preformulated hot melt adhesive, was added and mixed for a further 30 minutes.

The Kraton KD-1161NS is a blend of linear styrene/isoprene/styrene triblock copolymer and linear styrene/isoprene diblock copolymer. Such a material is available from Shell Chemical Company and has a bound styrene content of about 15% and a diblock content of 17%. The mixture of tackifying resins used was a cyclopentadienyl resin, Escorez 2203LC, available from Exxon Chemical, and Adtac LV-E, a C5 synthetic hydrocarbon resin available from Hercules Chemical Company. The Irgafos 168 is an organophosphite stabiliser available from Ciba while the Irganox 565 is a hindered phenolic antioxidant also available from Ciba.

Wt% of Each Raw Material	Ex 6	Ex 7	Ex 8
Polyisobutylene, Vistanex LMMH	28.0	28.0	28.0
GenuPectin USP 100	14.0	14.0	14.0
Sodium CMC, Blanose 7H4XF	14.0	14.0	14.0
Sodium CMC, Aqualon A-500	14.0	-	-
β-Cyclodextrin (Cavitron 82000)	-	14.0	-
Hydroxypropyl β-Cyclodextrin (Cavitron 82005)	-	-	14.0
Kraton D-1161NS	11.3	11.3	11.3
Adtac LV-E	6.0	6.0	6.0
Escorez 2203 LC	12.5	12.5	12.5
Irgafos 168	0.14	0.14	0.14
Irganox 565	0.07	0.07	0.07
Total	100	100	100

Physical Data	Ex 6	Ex 7	Ex 8
Reverse Tack, N/25mm	27.3	34.6	23.7
Peel Adhesion, 90°/SS, N/25mm	12.7	16.0	16.6
Shear, 0.5kg, minutes	129	190	237
Thickness, mm	0.67	0.75	0.70
Static Absorption, gm/sq.m./24hr	6265	3789	4648
Cold Flow, % increase/24hr/10kg	0.8	4.7	3.5
Integrity, %, 24hr.	50	78	74

Example 9

This example illustrates the preparation of a self adhesive acne pad using the teachings of the invention. The self adhesive pad contains a complex of β-cyclodextrin containing 10wt% tea tree oil, and available as EPICUTIN-TT

from Chemisches Laboratorium Dr. Kurt Richter GmbH, Berlin, Germany. This complex, although containing 10wt% tea tree oil, had no odour of the essential oil, which is liberated only by moisture.

Salicylic acid (20.0 gm) was added to polyethylene glycol PEG400 (40.0 gm) in a 100ml. screw capped bottle. The PEG400 is available from Clariant GmbH. The bottle was shaken overnight on an automatic shaker and most of the salicylic acid dissolved to make a viscous suspension.

Separately, a hot melt adhesive was prepared from Kraton KD-1161N, plasticised with a styrene-isoprene liquid rubber, LVSI-101. The Kraton KD-1161N is a blend of linear styrene/isoprene/styrene triblock copolymer and linear styrene/isoprene diblock copolymer. This material is available from Shell Chemical Company and has a bound styrene content of about 15% and a diblock content of 17%. The LVSI-101 is a block copolymer of styrene and isoprene having a styrene content of about 13% and an isoprene content of about 87%, a glass transition of about -60°C, a melt viscosity of about 2400 poises at 50°C and which is commercially available from Shell Chemical Company. Irganox 1010, a hindered phenolic antioxidant manufactured by Ciba, was used to stabilise the hot melt adhesive against thermal degradation during manufacture.

From the details given in PCT Application No: GB98/02069 the following procedure was followed. A Z-blade mixer was purged with nitrogen gas and heated to 160°C. The speed of the front, faster blade was 30 rpm. Kraton KD-1161N (100gm) and Irganox 1010 stabiliser (4.0gm) were charged to the mixer at 160°C, and the mixer was started. After mixing for 5 minutes,

the rubbery crumb coalesed, and 50gm of liquid rubber styrene-isoprene copolymer, LVSI-101, was added with continued mixing and nitrogen purging. After a further ten minutes, the temperature was raised to 170°C and the mixer front blade speed increased to 47rpm. The LVSI-101 had at this point completely mixed with the rubber, and a further 50gm of LVSI-101 was added. Ten minutes later, after blending of the second portion of the LVSI-101, a further 49gm of LVSI-101 was added, and mixed for a further 10 minutes. In this way, approximately 50gm portions of the charge of LVSI were added every 10 minutes until a total of 400gm of LVSI-101 had been added. After a further 15 minutes, the intermediate adhesive was dumped from the mixer. The total time for this operation was about 90 minutes.

Formula 2-18A	Gm.
LVSI-101	400
Kraton KD-1161N	100
Irganox 1010	4

From this intermediate mixture, referred to as Formula No 2-18A in the Tables, a finished hydrocolloid adhesive was made having the formula shown below. The Pectin USP100, NaCMC Blanose and the Vistanex polyisobutylene were mixed in the Z-blade mixer at 80°C. and the intermediate adhesive 2-18A was added at 100°C. The mixer was then cooled back to 80°C and the suspension of salicylic acid in PEG400 was added. After further mixing for 15 minutes, the mixer was cooled to 60°C, and the Epicutin-TT was added with additional mixing for 15 minutes, prior to dumping the adhesive.

Example 9	Gm.
2-18A	182.35
Vistanex LMMH	72.95
Pectin USP100	35.35
NaCMC, Blanose	35.35
PEG400	16.00
Salicylic Acid	8.00
Epicutin-TT	50.00
Total Weight	400.00

The adhesive thus contained 2.00wt% salicylic acid and 1.25wt% of tea tree oil. The adhesive was pressed between two sheets of silicone release paper in a hydraulic press at 90°C. After removing one protective silicone release paper, the sheet of adhesive was laminated to a non woven fabric, previously transfer coated with a medical grade acrylic adhesive which acts as a tie coat to bond the hydrocolloid adhesive to the fabric. Discs of the construction, 2cm in diameter, were cut. Four of the adhesive discs were applied over five days to an acne lesion on the back of a 41-year-old Caucasian female with a long history of pre-menstrual acne outbreaks. The following observations were made:

Day	No. of Disc	Adhesion level	Condition of intact skin under disc after removal	Assessment of acne after removal of disc
Day 0	-	-	-	Painful raised pimple (initial assessment)
Day 1	Disc 1	Excellent	No sign of skin redness	Pimple redness reduced, Small comedone visible
Day 2	Disc 2	Excellent	No sign of skin redness	Raised pimple reduced
Day 3	Disc 2	Excellent	(Disc left for 48 hrs)	-
Day 4	Disc 3	Excellent	Very slight sign of skin redness	Drying of lesion, comedone disappeared
Day 5	Disc 4	Excellent	No sign of skin redness	Further drying of lesion

There was a significant visual improvement over the five days in the healing of the treated acne lesion compared to an untreated lesion on the same patient. The patient found that the discs had excellent adhesion to skin. The disc, even though covered by clothing, never became adhered at its edges to the clothing, demonstrating the excellent cold flow performance of this adhesive patch. The patch gave satisfactory control of acne lesions during the peri-menstrual time.

Examples 10 - 12

These examples demonstrate the odour absorbing properties of adhesives made according to the teachings herein. An adhesive, Example 10 to be used as a control in the following experiments and containing no cyclodextrins, was made according to our copending Application number PCT No: GB98/02809 and Examples 11 and 12 were made according to the teachings herein. The compositions of the three adhesives are given in the Table below:

Amount in Mix, wt%	Example 10	Example 11	Example 12
Kraton D-1161NS	11.3	11.3	5.9
Adtac LV-E	6.0	6.0	-
Escorez 2203 LC	12.5	12.5	-
Irgafos 168	0.14	0.14	-
Irganox 565	0.07	0.07	-
Vistanex LMMH	28	28	28
LVSI 101	-	-	23.7
Irganox 1010	-	-	0.4
Cavitron 82000	-	14	-
β-Cyclodextrin W7	-	-	14
Methyl substituted β-Cyclodextrin W7M1.8	-	-	14
Sodium CMC	14	14	-
Pectin USP100	14	14	-
Aquasorb A-500	14	-	14

The three adhesives were pressed to a thickness of about 1mm between two pieces of release paper using a hydraulic press held at 90°C. The sheets were then laminated to 25μ polyurethane film, previously coated with a medical grade acrylic adhesive to act as a tie coat between the film and the hydrocolloid adhesive.

Using the MVT cups described above under the Section "Test methods - Static absorption of hydrocolloids", the pressed and laminated samples from Examples 10 - 12 were adhered to the flanges of cups that contained 30 ml aqueous NaCl solution (0.9%wt). Exactly as described in the Test method, the cups were turned upside down, put in the oven at 37°C. for 24 hours and then cooled down. The hydrocolloids were removed from the cups, the circular saline-saturated portions were cut out from the remainder of the hydrocolloid pad, and each circle was

placed in the bottom of a wide-mouthed screw-capped 1l. jar, hydrocolloid side up.

Each of the saline soaked pads was inoculated with 5µl of n-butyric acid using a microsyringe, and the caps screwed tightly on the jars. The n-butyric acid is a strong smelling compound found, together with other fatty acids, in odiferous wounds. After 24 hours, the three samples were smelled in turn by four panelists, who rated each of the three samples according to intensity of odour.

First, the panelists smelled each jar and ranked them according to strength of odour, from strongest odour to weakest. The panelists then smelled each jar a second time, and scored each on a scale of 0-5, 0 being no smell and 5 being the strongest.

These ratings of 0-5 for each adhesive were then rank ordered among the adhesives for each panelist, and the rankings for each adhesive were summed among the panelists. The following data were obtained, where 12 is the maximum possible score (highest odour), and 4 is the lowest possible score (lowest odour).

Sample	Odour Level, Sum of Rankings, Σ
Example 10	12
Example 12	7
Example 11	5

The data showed that little or no odour of n-butyric acid was detected with the adhesives of Examples 11 and 12, while the adhesive from Example 10, which contains no cyclodextrin

material, retained the strong, unpleasant odour of n-butyric acid after 24 hours.

Example 13

This example shows the incorporation of cyclodextrins into a pressure sensitive adhesive formed from a hydrogel.

A glass vessel of 250ml capacity is tared on an electronic balance and polyvinyl alcohol (0.1gm) is added, followed by 5ml of deionised water. γ-cyclodextrin (0.5gm) and α-cyclodextrin (0.5gm) are then added and the mixture is stirred vigorously until all the solid materials are dissolved. The following monomers are then introduced into the glass vessel: N,Ndimethyl acrylamide (10gm), methoxypolyethylene glycol methacrylate (MW400, 1gm), polyethylene glycol dimethacrylate (0.10gm), Daracure 1173 (CIBA, 0.4gm) and 1:2 propylene glycol (1gm).

The ingredients are mixed thoroughly and coated in a thin layer on to a piece of silicone release paper. The coated paper is passed 12 times beneath a FUSION F300S UV curing apparatus on a conveyor belt running at a speed of about 4m/min. The bulb used is 15cm long and emits light of wavelength λ in the range 200 - 400nm.

A self-supporting sheet of aqueous tacky gel is produced, which is flexible enough to be removed from the release paper, and which shows good adhesion to dry skin.

CLAIMS:

1. A pressure sensitive adhesive composition comprising a rubbery continuous phase with a discontinuous phase distributed therein, characterised in that the discontinuous phase comprises a cyclodextrin in an amount of 0.1 to 65 wt %, based on the total composition.

2. An adhesive composition according to claim 1 wherein the discontinuous phase also comprises a hydrocolloid other than cyclodextrin.

3. An adhesive composition according to claim 1 or 2 wherein the cyclodextrin is present in an amount of at least 5 wt % based on the total composition.

4. An adhesive composition according to claim 3 wherein the cyclodextrin is present in an amount of at least 10 wt % based on the total composition.

5. An adhesive composition according to any preceding claim wherein the continuous phase comprises up to 50 wt.% of polyisobutylene as a major component.

6. An adhesive composition according to any preceding claim wherein the continuous phase contains up to 15 wt.% of a rubbery copolymer of styrene or a substituted styrene as a major component.

7. A pressure sensitive adhesive composition comprising an aqueous hydrogel, characterised in that the adhesive also contains a cyclodextrin in an amount of 0.1 to 65 wt %, based on the total composition.

8. An adhesive composition according to any preceding claim which additionally contains an active ingredient.

9. An adhesive composition according to claim 8 wherein the active ingredient is complexed with the cyclodextrin.

10. An adhesive composition according to claim 8 or 9 wherein the active ingredient is selected from hydroquinone, menthol, salicylic acid, antibacterial agents, antifungal agents, essential oils and fragrances.

11. A medical or surgical appliance comprising a substrate on which is formed a layer of a pressure- sensitive adhesive composition according to any preceding claim.

12. An appliance according to claim 11 in the form of a wound dressing.

13. An appliance according to claim 11 which comprises a skin barrier.

14. An appliance according to claim 13 in the form of an ostomy appliance.

15. An appliance according to claim 13 in the form of a transdermal delivery patch for an active ingredient.

16. An appliance according to any one of claims 11 to 15 wherein the substrate includes a backing comprising non-adhesive waterproof film.